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A.M.A. ARCHIVES OF SURGERY

Sixth Scientific Meeting of North American Chapter of International Cardiovascular Society, San Francisco, June 21, 1959

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Study of Elasticized Dacron as Arterial Prosthesis
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Evaluation of Thromboendarterectomy in Treatment of Obliterative Arterial Disease
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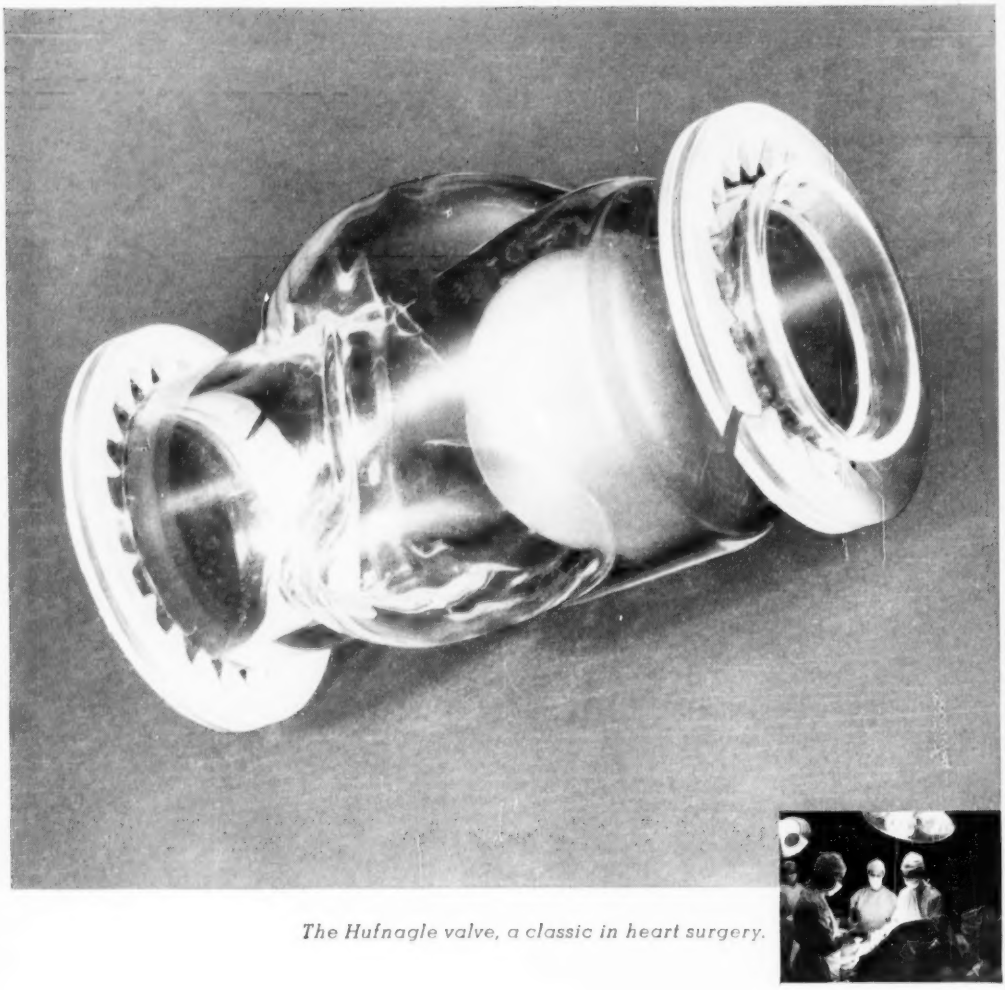

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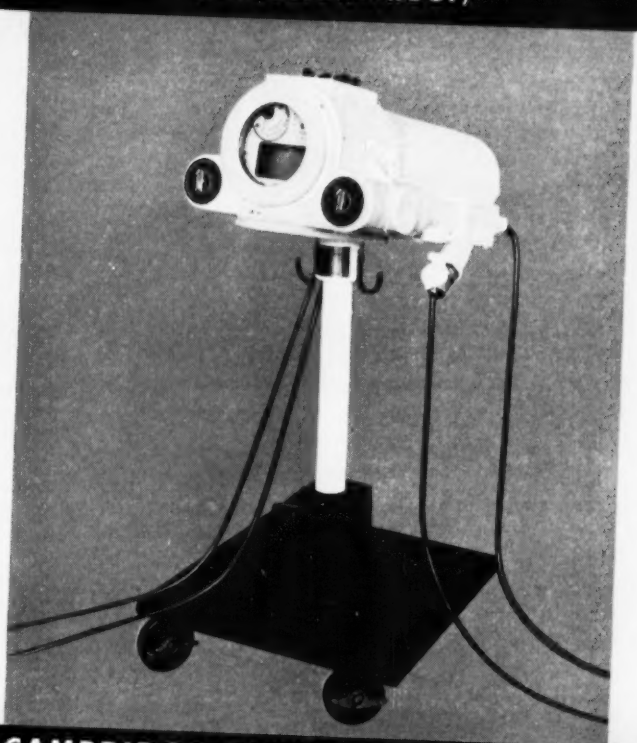

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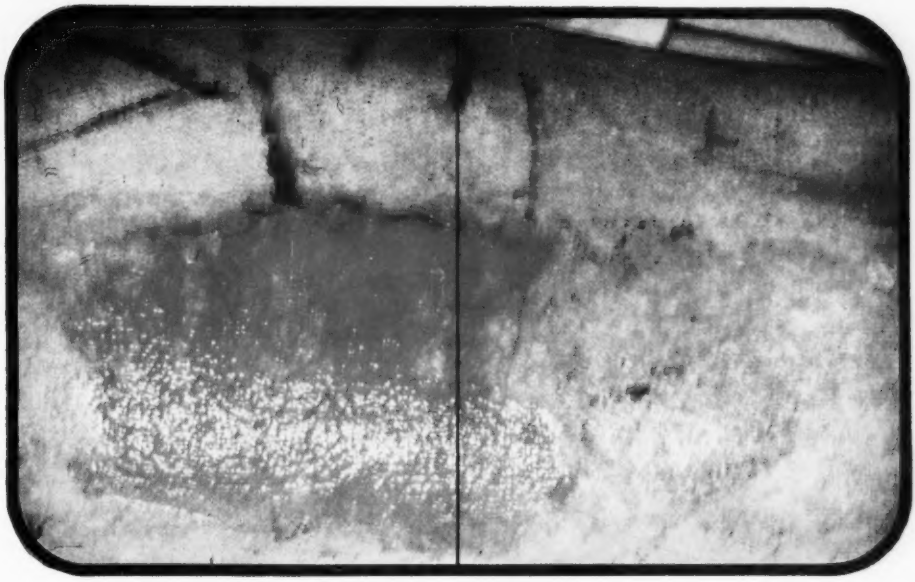

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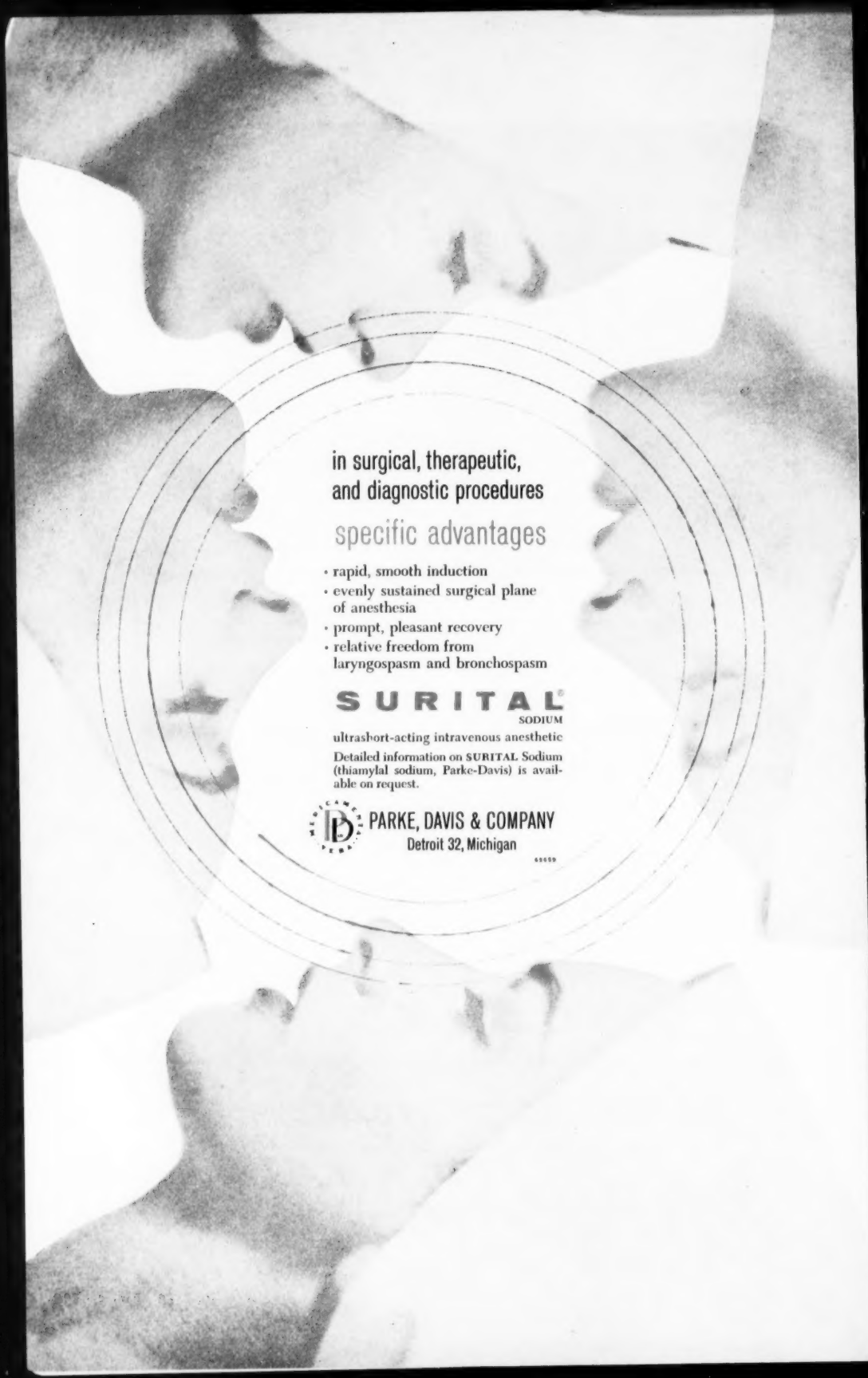
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Human Values in Medicine

HARRIS B. SHUMACKER JR., M.D., Indianapolis

The North American Chapter of the International Cardiovascular Society confers upon its president an unusual opportunity, that of retaining office over a two-year period. This carries with it the unique responsibility of delivering two presidential addresses. Last year I spoke on a scientific subject. This year I propose to speak in a more philosophic vein.

Each generation owes a debt to society, an obligation to see to it that the next can live an even fuller, richer, more rewarding life than it has enjoyed. We in medicine have a particular responsibility to the medical profession of the future and to the people it serves. How can we make sure that succeeding generations of medical graduates are well prepared for the opportunities and responsibilities which will be theirs?

The proper education of young men and women in medicine can be accomplished only if certain basic requirements are met. There must be a faculty composed of persons competent in their respective fields, dedicated to their tasks, and capable of stimulating the student to take full advantage of the learning opportunities available to him. It should, in my opinion, comprise in substantial numbers persons who themselves are actively engaged in investigations aimed at expanding the frontiers of knowledge, since such men are most likely to incite in the student that ideal attribute of thinking for himself, of inquiring restlessly into the truth or fallacy of every concept. Such men, too, are most apt to impart to students a desire not only to assimilate and utilize past and current knowledge but to make a personal effort to extend it. The faculty must, furthermore, be composed of persons who set a good and convincing example in the pursuit of their daily tasks. They must love their work and the patients they treat. Obviously, they must have the tools with which to work: adequate patient material, laboratories, and libraries.

No matter how capable the staff and fine the facilities, the mission cannot be accomplished without a receptive and talented student body. What sort of person should the student be? He must have good native intelligence. He must have a burning interest in becoming a physician. He must have a good basic background in the physical, chemical, and biologic sciences. He should have, in addition, a broad education in the humanities in order to be able to carry out his work with maximal enjoyment and to integrate his professional life into the life of the community. Though such qualities and accomplishments are not easily assessed, they can be fairly accurately evaluated. The student's scholastic record, his performance in certain aptitude and intelligence tests, his response to questioning during a personal interview, letters from

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From the Department of Surgery, Indiana University School of Medicine.

Presidential address delivered at the Sixth Scientific Meeting of the North American Chapter of the International Cardiovascular Society, San Francisco, June 21, 1958.

his instructors and advisors, altogether permit a reasonable estimate of his past performance and future promise. If carefully selected, he is likely to do well and to help medicine maintain its forward movement.

I am convinced, however, that, in general, the prospective medical student should have other attributes, more difficult to define and harder to evaluate. I refer to his human values. I would be the first to admit that a bright and inquisitive student of an asocial, or even antisocial, nature can find a niche in medicine where his capacities may prove worth while. He may, for example, make significant contributions in the laboratory. The vast majority of physicians, however, are destined to rub shoulders with humanity, and particularly with the sick. They should have a real love of mankind, a compassion for suffering, a deep understanding of the fears and doubts and hopes of the ill and injured and of their families and friends. These are qualities which are difficult to estimate in the candidate for admission to medical school. I know of no test which will accurately evaluate them. One may know the correct answers to queries and be devoid of deep feeling and appreciation of their significance, just as a person may recite the best rules of conduct and yet be unrefined or even uncouth.

These human qualities are essential, I feel, in those who assume the difficult and rewarding task of treating patients. With proper increasing emphasis on the scientific progress of medicine, perhaps we have neglected somewhat the importance of these human values. Yet their significance in every branch of medicine is obvious. Patients are naturally concerned about their illness. Most of them know little about its nature. What information they have is likely to have been gained from lay persons and lay publications and to be somewhat in error. Justifiably, they wish to have this cloud of doubt removed and to understand something about the nature of the trouble which afflicts them, about pertinent methods of study and management and the possibilities of relief. They have other problems relating to their families and their work. All of these must be taken into consideration and dealt with by every conscientious physician and surgeon. The scope of these personal human problems has recently been extended because of the marked reduction of infant mortality, at one extreme, and increased longevity, at the other. More infants are surviving with congenital malformations which prove a distressing problem to them and to their parents. The aged, on the other hand, present certain special difficulties both for themselves and for their relatives.

My experiences, of course, are limited largely to the surgical treatment of patients. I should like to illustrate some of the problems to which I refer by dealing specifically with the preoperative preparation of the patient and his family. No matter how little the risk involved, I cannot condone the attitude of simply slapping a patient on the back, or his parent, and saying "We shall operate and everything will be all right." Let us consider an interview with the parents of a child who needs cardiac surgery. Let us suppose the child is a healthy-looking, asymptomatic youngster with coarctation of the aorta. We know that the decision to operate is the only sound one. We are aware of the ultimate poor prognosis without treatment, the successful restoration of normal cardiovascular dynamics by operative correction, the minimal risk involved. When first confronted with the problem, the parents, in contrast, inevitably think of the terrifying responsibility they face in committing a seemingly well child to anesthesia and surgery. They deserve a patient, painstaking explanation of the condition which exists, the data upon which prognosis without treatment is based, the general objectives of the proposed operation, the evidence concerning the risk involved. Before the child is scheduled for operation, the parents must be as thoroughly convinced as we that they have made the correct choice, so thoroughly convinced that even if their child is the rare one who succumbs, they will know deep in their

heart that they have made the right decision. This is all the more important when the child faces a graver operation with a higher risk, for example, open cardiotomy for repair of a ventricular septal defect associated with marked pulmonary hypertension and vascular sclerosis. These preoperative conversations are never useless, and, on occasions, they may prevent psychic disaster later on. I do not mean to intimate that every physician and surgeon must be a competent psychiatrist. On the other hand, a warm manner and a sympathetic understanding may do a great deal in our day-to-day work to obviate the need for skilled psychiatric aid. I often feel that the surgeon who does not spend more time talking with and listening to his patients and their families than he does in the operating room is derelict in his responsibilities. We must always keep in mind the old axiom that it is the patient we are called upon to treat and not just the disease from which he suffers.

The same human qualities that are required in good medical care should also make us good citizens. Knowing as we do from daily contacts the weakness and strength of our fellow men, their fears and hopes, their assets and burdens, we should be leaders in liberal thought in our communities. Knowing so much better than others that color differences are truly only skin deep; that suffering, aspiration, and love are common to all religious groups, we should be stalwarts against intolerance and reaction. Working daily with the fruits of scientific and intellectual progress, we should be in the forefront of all progressive movements. Obviously, I refer to the broad principles of human and social relationships and not to specific tenets of existing political organizations.

We in medicine are in a unique position. We live in an atmosphere which knows no national barriers, no secrets, no enmities. As soon as a new contribution is made in any country, it is immediately published to be used in any spot on the globe. This has always been true not only of our friends and allies but of our potential adversaries as well. The benefits to mankind are obvious. Perhaps government leaders might review with profit the result of this free interchange of ideas. Our position, however, is unique in another respect. Here I come finally to one of the objectives of this Society, for I am sure it was conceived not only to bring about a free and intimate interchange of scientific accomplishments and ideas among those of us in the various member nations interested in cardiovascular progress but to permit us to know one another as individuals as well. Many of us are provided with the rare opportunity to know personally many of our colleagues in other nations, some intimately, some less well. We find that they have the same interests and objectives as we. Furthermore, through our travels, we become acquainted with lay people in other countries and find that they, too, have the same qualities we observe in our compatriots. From our acquaintance with them we realize that, though government policies may vary, people everywhere have the same yearning for a peaceful, happy, healthy, productive life.

I am confident that we and the physicians who succeed us will continue to meet our responsibilities. I am convinced we can do so best by holding high human as well as scientific values in medicine.

Indiana University Medical Center, 1040-1232 W. Michigan St. (7).

Exercise and Limb Circulation in Health and Disease

TRAVIS WINSOR, M.D.; CHESTER HYMAN, Ph.D., and J. HOWARD PAYNE, M.D., Los Angeles

The distribution of blood to the several tissues of the extremities during rest and exercise has been the topic of much discussion. It is usually assumed that the arteries of the healthy extremity not only can supply the resting needs of the several tissues but can easily carry the extra blood required to perfuse the dilated blood vessels in exercising muscle without depriving the skin or other tissues of the extremity. In arterial occlusive diseases, at least one group of authors has considered the possibility that the arterial blood supply is in fact inadequate to meet the needs of the exercising tissues. According to this concept, the satisfaction of the excess circulatory needs of the exercising muscle is achieved at the expense of the other tissues. If this is the case, the use of exercise in the treatment of peripheral vascular disease may be harmful.

The present series of studies was designed to obtain information concerning the effects of exercise of the calf muscle upon the circulation in the toe, foot, ankle, and calf. Knowledge of these circulatory changes was then used to devise a simple clinical test which often differentiates between leg pain due to arterial occlusive disease and that arising from other vascular or nonvascular causes, e. g., myositis or arthritis. In addition, an attempt has been made to apply objective criteria to the evaluation of exercise as a therapeutic procedure in peripheral vascular insufficiencies.

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From the Departments of Medicine, Physiology, and Surgery, University of Southern California School of Medicine, and the Heart Research Foundation and the Foundation for Surgical Research.

Methods and Materials

The following studies were carried out on 50 normal subjects with an average age of 40 (range, 21 to 62) and 25 patients with an average age of 52 (range, 43 to 74) who had arterial occlusive disease involving the large arteries (aorta, iliac, femoral, or popliteal). All patients had arteriosclerosis obliterans and intermittent claudication and were ambulatory. The studies were carried out in a peripheral vascular laboratory after a rest of 15 minutes. The subjects were covered with a wool blanket at a room temperature of 24±1 C. The studies were divided into four groups, which involved (1) the toe, (2) the foot, (3) the ankle, and (4) the calf. The instruments employed for these studies were the digital plethysmograph,[1] the segmental plethysmograph,[2] the Brown recorder and boot plethysmograph,[3] and gamma-ray spectrometer and recording rate meter. Exercise was carried out with a foot ergograph, which consisted of a stirrup which was fastened around the ball of the foot. The foot was extended against the stirrup to lift a 10 lb. weight through a distance of 4 in. at intervals of one and a half seconds in rhythm with a metronome. The work done was added automatically. The patients were urged to exercise for a four-minute period, or until pain prevented further movement of the foot. The normal subjects performed 800 ft.-lb. of work in four minutes without pain. Immediately after cessation of exercise the stirrup was disconnected from the foot, and within 15 seconds measurements of the circulation were made.

The maximum pulse (oscillometric index) was recorded using the segmental plethysmograph by varying the cuff pressure to give the largest pulse amplitude with the leg at rest. Muscle blood flow was measured using the segmental plethysmograph cuff (8×40 cm.) inflated to 20 mm. Hg around the calf, a venous occluding cuff above the knee inflated to about 70 mm. Hg, and an arterial occluding cuff at the ankle. All other measurements were made by procedures previously described.[1-3]

Effect of Exercise on Various Measurements of the Circulation of the Leg

		Resting			15 Sec. After Exercise		1 Min. After Exercise	
		No.	Mean	Range	Mean	% of Resting	Mean	% of Resting
I	Toe flow—toecuff (Cu. mm/4 cc/sec.)							
	Normal	5	30.0	20-52	27.0	90	36.5	122
	Disease	10	12.0	8-28	1.5	13	2.0	17
	Toe flow—ankle cuff (Cu. mm/4 cc/sec.)							
	Normal	5	10.0	8-14	9.2	92	12.7	127
	Disease	10	7.0	4-13	1.0	14	1.4	20
	Pulse height, toe (Cu. mm/4 cc.)							
	Normal	30	6.0	4-9	5.5	92	7.0	177
	Disease	15	4.0	1-6	1.0	25	1.5	33
	Skin temperatures, toe, C							
	Normal	30	31.0	28-34	30.0	97	30.5	98
	Disease	15	28.0	26-29.5	27.5	98	27.5	98
II	Foot flow (Cc/100 cc/min.)							
	Normal	5	4.0	2.8-7.8	4.0	100	16.0	400
	Disease	5	2.0	0.9-4.2	0.5	25	0.6	30
III	Ankle maximum pulse (Cc/pulse)							
	Normal	15	0.5	0.3-0.7	0.4	80	0.5	100
	Disease	15	0.2	0.09-0.3	0.02	10	0.04	20
	Blood presure, systolic, ankle (Mm. Hg.)							
	Normal	15	120	100-145	108	90	110	92
	Disease	15	78	40-90	30	38	35	45
IV	Calf pulsation (Cc/pulse)							
	Normal	10	1.3	1.0-1.9	1.5	115	1.4	108
	Disease	10	0.8	0.4-1.1	0.9	113	0.8	100
	Calf flow (Cc/100 cc/sec.)							
	Normal	10	4.0	3.1-6.8	8.0	200	16.0	400
	Disease	10	3.8	2.1-4.5	4.0	105	8.4	221

Results

I. Toes.—A. Flow: The data with reference to changes in blood flow through the toes are summarized in the accompanying Table. In the normal subjects the mean blood flow measurements made 15 seconds after exercise were not substantially different from the control values, while there was a small increase in the mean of the values obtained 1 minute after exercise. In contrast, the blood flow through the toes of the patients fell to 13% of the control value 15 seconds after exercise, and a low level was maintained for at least 1 minute. Examples typical of a normal subject and of a patient with peripheral arteriosclerosis are shown in Figures 1 and 2. There was no evidence of differences in this response measured after sympathectomy in a small group of patients. Substantially the same results were obtained when blood flows were measured by venous occlusion at the level of the ankle or the level of the toe.

The blood flow debt or credit measured at the toe with the toe-occluding cuff was studied in five normal subjects and in five patients with peripheral arterial disease (Fig. 3). The blood flow debt or credit was calculated every minute for a 10-minute period prior to exercise and every minute for a 10-minute period immediately following exercise. The difference between the volumes of flow for the two 10-minute periods was then determined. In the normal subjects the total flow following exercise was greater on the average than the preexercise values (area under the curve), while in the diseased patients the postexercise flow was,

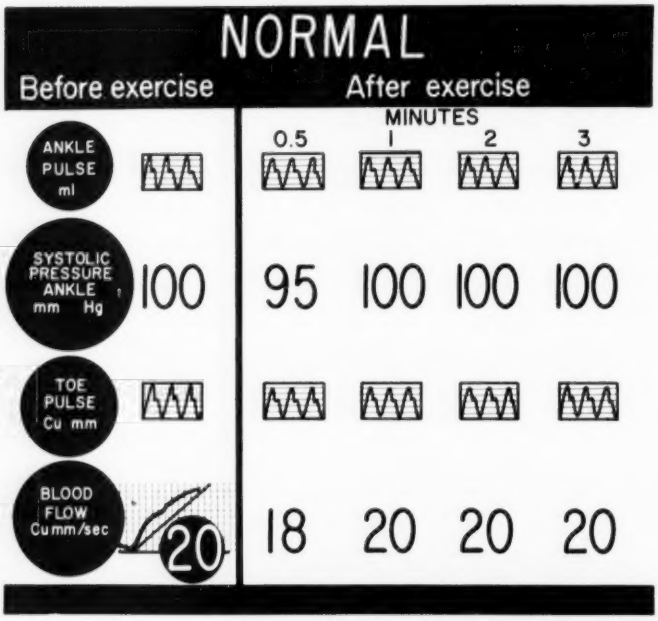

Fig. 1.—Ankle pulse, systolic blood pressure at the ankle, toe pulse, and blood flow at the toe in a normal subject before and after exercise. (See text for explanation.) Reproduced from Winsor, T.: Peripheral Vascular Diseases: An Objective Approach, by permission of Charles C Thomas, Publisher, Springfield, Ill.

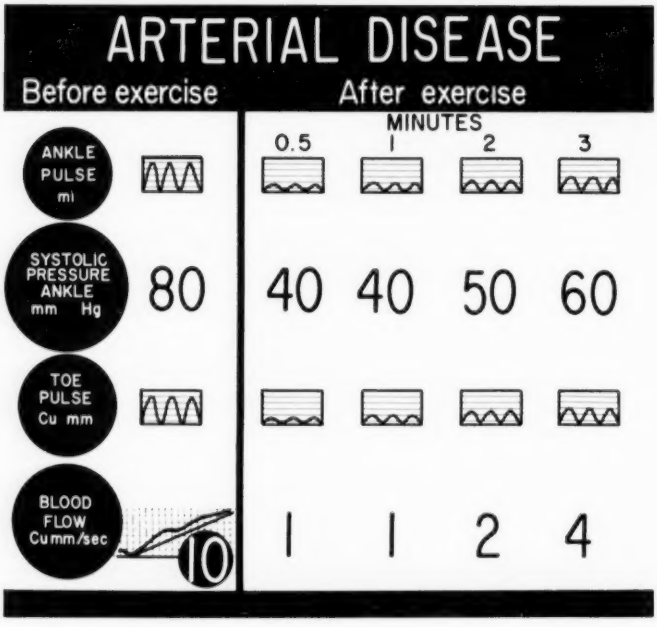

Fig. 2.—Ankle pulse, systolic blood pressure at the ankle, toe pulse, and blood flow at the toe in a patient with peripheral arterial disease before and after exercise. (See text for explanation.) Reproduced from Winsor, T.: Peripheral Vascular Diseases—An Objective Approach, by permission of Charles C Thomas, Publisher, Springfield, Ill.

on the average, less than the preexercise flow. There were no significant differences in five patients tested before and after lumbar sympathectomy.

B. Pulse Height (Table): In the normal subjects the mean of the pulse heights for the toe made 15 seconds after exercise was not substantially different from the control

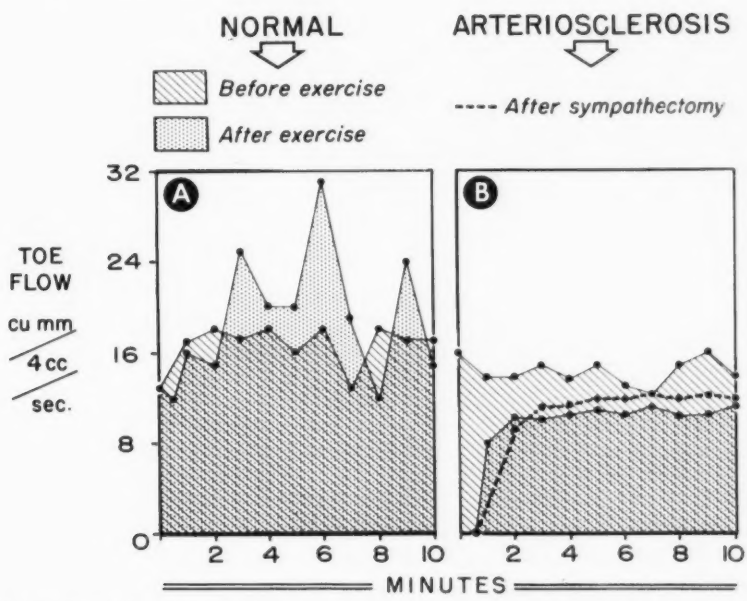

Fig. 3.—Blood flow debt and credit in a normal subject who showed a blood flow credit after exercise (*A*), as compared with a patient with arteriosclerosis who showed a blood flow debt after exercise (*B*). The results in the arteriosclerotic patient were similar before and after a sympathectomy.

value, while there was a small increase in the mean value obtained 1 minute after exercise. In contrast, the pulse height measured in the toes of the patients with occlusive vascular disease fell 15 seconds after exercise to 25% of the control value, and a low level was maintained for at least 1 minute. Typical results from a normal subject and from a patient with peripheral arteriosclerosis are shown in Figures 1 and 2. There was no significant difference in response measured after lumbar sympathectomy in a group of five patients.

C. Skin Temperatures (Table): Both in normal subjects and in patients with arteriosclerosis obliterans there was a slight decrease in temperature of the toes 15 seconds after exercise, which was still present after 1 minute. No significant differences were observed between the normal and the diseased subjects or before and after sympathectomy.

II. Foot Flow (Table).—In the normal subjects the mean of the blood flow measurements at the foot made 15 seconds after exercise was not different from the control value, but there was a substantial increase in the mean of flows measured after 1 minute. In contrast, the blood flow through the foot of the patients with occlusive vascular disease fell 15 seconds after exercise to 25% of the control and remained at a low level at 1 minute. There was no evidence of difference in this response measured after sympathectomy in five patients.

III. Ankle.—A. Maximum Pulse (Table): In the normal subjects maximum pulse heights measured at the ankle 15 seconds and 1 minute after exercise were not substantially different from the control values. In contrast, the maximum pulse height in the patients with occlusive vascular disease fell 15 seconds after exercise to 10% of the control value, and at 1 minute the reading was still only 20% of the control. Examples of a normal subject and of a patient with peripheral arteriosclerosis are shown in Figures 1 and 2. Substantially the same results were obtained when maxi-

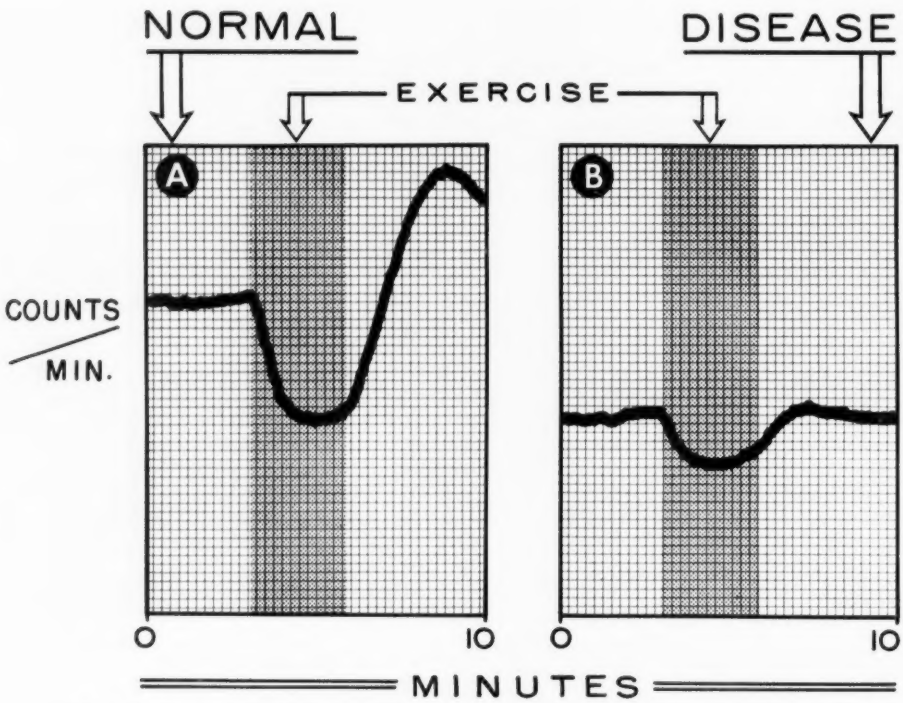

Fig. 4.—Effect of exercise on calf muscle circulation shown by the recording made from calf muscle before, during, and after exercise after intravenous injection of radio-iodinated (I^{131}) albumin. In normal subjects a postexercise increase in count is seen (*A*). This is absent or small with disease (*B*).

mum pulse heights were obtained in five patients after sympathectomy.

B. Systolic Blood Pressure (Table): In the normal subjects the means of the systolic blood pressures at the ankle 15 seconds and 1 minute after exercise were not substantially different from the control values. In contrast, the systolic pressures of the patients with vascular disease fell 15 seconds after exercise to 38% of the control value. The pressures were 45% of the control value at one minute. Examples of a normal subject and of a patient with peripheral arteriosclerosis are shown in Figures 1 and 2. There was no evidence of differences in this response measured after sympathectomy in five patients.

IV. Calf.—A. Pulsation (Table): In both the normal and the diseased subjects the calf pulsations increased slightly 15 seconds after exercise, and at 1 minute the pulsations were slightly above or similar to the average control readings.

B. Blood Flow (Table): In the normal and in the diseased subjects an increase in blood flow was recorded 15 seconds and 1 minute after exercise. The average increase in the normal group was greater than that in the diseased group. It is noteworthy that in no patient did a decrease in circulation occur with this procedure.

C. Plasma Content of Calf (Fig. 4): RISA (radio-iodinated [I^{131}] serum albumin [human]) was injected intravenously, and, after stabilization of the count had occurred, scintillation counts were made over the calf. Definite differences in the effect of exercise in health and in disease were observed. In five normal subjects the count decreased significantly with exercise but rose above the control value during rest. In the patients wih arteriosclerosis obliter-

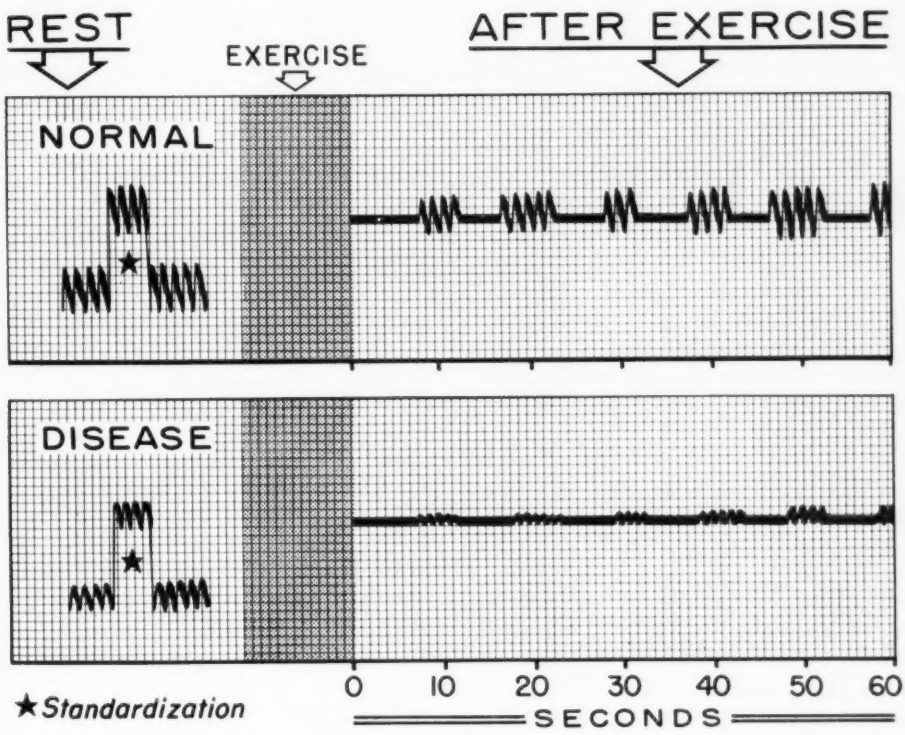

Fig. 5.—Exercise tolerance test in a normal subject and in a patient with arteriosclerotic obliterative disease.

ans, a slighter decrease in count occurred during exercise, and the postexercise count did not increase materially over that of the control resting level.

Ankle Pulsations Employed as Test for Peripheral Vascular Disease

Of the variety of tests which were performed in these studies, the segmental plethysmogram recorded at the ankle before and after exercise seemed practical as a clinical test for the detection of arteriosclerosis obliterans. The test can be carried out with a single or a multiple channel instrument. The technique is as follows: Employing a two-channel instrument, cuffs are applied to the ankles in the usual manner, and the maximum pulses at the ankles are recorded by selecting the proper cuff pressure (*vide supra*). The gain of the instrument is adjusted so that the amplitude of pulsation is 10 mm. A control record is taken with a slow paper speed (2.5 mm. per second). The cuffs are deflated, and the color of the feet is noted. The technician stands at the foot of the bed and places the palms of his hands against the soles of the patient's feet. The patient is then encouraged to exercise by dorsiflexing his feet once a second against resistance until he complains of pain or is unable to continue exercise because of weakness of the muscle groups. At this point the cuffs are again inflated to the previously determined pressure, and pulsations are recorded every 10 seconds for 1 minute (Fig. 5). The results for normal subjects and for patients studied in this way are shown in Figure 6 and in the Table. For the normal subjects shown in the Table the average 15-

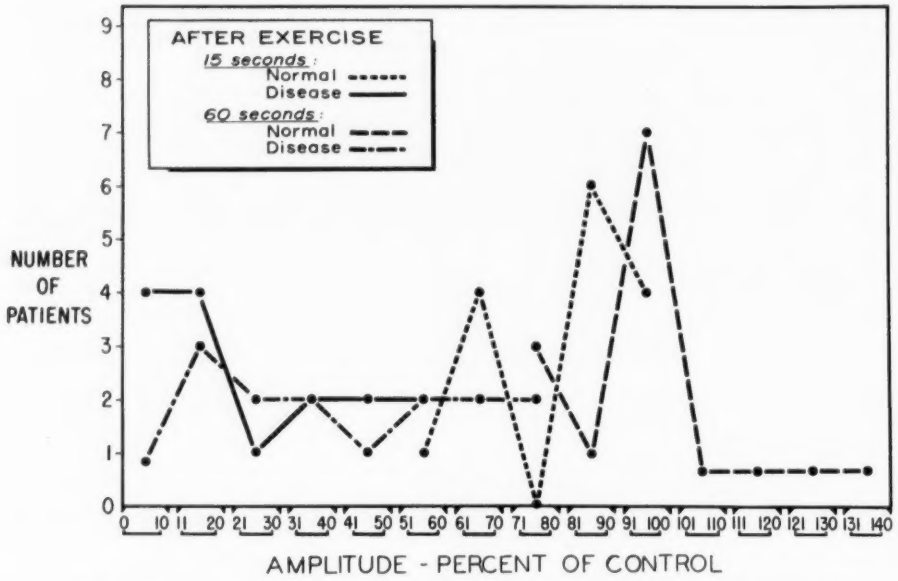

Fig. 6.—The amplitude of the ankle pulse was determined before and after exercise, and the per cent of the control amplitude was plotted against the number of patients studied. In the normal subjects, 60 minutes after exercise the ankle pulse in most subjects was similar to that of the control, whereas in the disease group the reading at 1 minute after exercise was significantly reduced below that of the control.

second reading was 80% of the control, whereas the average 1-minute reading was 100%. With arteriosclerosis obliterans patients at 15 seconds there was a marked decrease to an average of 10% of the control value, and the average reading at 1 minute was 20% of the control value.

Comment

The results obtained in the normal subjects indicate clearly that the normal artery can supply all of the blood needed by the exercising muscle without depriving any other tissue. This is apparent from the fact that the blood pressure measured at the ankle changes only slightly after exercise, so that the pressure available for perfusion of the tissues below this point remains normal. Measurements of unaltered blood flow through the foot and through the toe after a period of exercise are even more direct evidence of the adequacy of the circulation in these tissues. Hilton [4] has shown that normally exercise causes dilatation of the artery proximal to the exercising muscle, increasing the circulation to the distal parts of the limb. In contrast, in patients suffering from arterial occlusive diseases, exercise of the calf muscle results in a significant drop in the pressure measured at the ankle, strongly suggesting a diversion of blood from the artery through the widely dilated blood vessels of the exercised muscle. This diminished pressure for perfusion is manifested in the decrease in the blood flow through the foot and through the toes of the diseased patient. The decrease in pulse height at the ankle, as measured by the segmental plethysmographic technique described here, is most likely explained on the basis of the diminished arterial pressure at this point. If the mean arterial pressure falls significantly, the arbitrarily determined cuff pressure becomes excessively great, and the recorded arterial pulsations are correspondingly diminished.

The decrease in the circulation at the level of the ankles afer exercise in diseased patients is sufficiently dramatic to allow this phenomenon to be employed as a diagnostic test for peripheral arteriosclerosis. A somewhat similar test has been suggested by Ejrup, who records systolic and diastolic blood pressures at the ankles after exercise and shows clearly a decrease in pressures with arteriosclerotic obliterative disease.[5] In the test herein described, a cuff is inflated to a pressure which is near mean pressure, and which is the largest pulse that can be obtained from any of several cuff pressures. The cuff is not inflated during exercise. After exercise the cuff is inflated to the control pressure. The amount of fall in pulse amplitude in 15 seconds and at 1 minute is noted. In a patient with disease of the large arteries of the leg exercise causes the arterial pressure at the ankle to fall, so that the cuff pressure will exceed that of the ankle pressure. If disease is great, the ankle pulse may disappear completely and the time required for the return of the ankle pulse to the resting level may be many minutes. Often the ischemic appearance of the limb after exercise is dramatic.

The use of sympathectomy to modify the blood flow in the diseased limbs is based theoretically on two modes of action: (1) increase in collateral flow and (2) decrease in vasoconstrictor tone in the skin.[6] It is now well established that sympathectomy does not influence the blood flow response to exercise.[7] The failure of this procedure to modify any of the measurements taken after exercise in the present study suggests that this procedure does not increase the collateral blood flow into a limb whose large arteries are occluded and casts further doubt on the efficacy of this procedure as a means of improving significantly the collateral circulation; however, numerous studies have demonstrated the value of sympathectomy as a means of decreasing vasoconstrictor tone in the skin.[8] These observations have some bearing on the treatment of patients with peripheral vascular disease. It would seem detrimental to the skin and to the distal portions of the limbs for patients with arteriosclerosis obliterans to walk excessively or to exercise to the point where blood flow debt occurred. It would seem important to weigh carefully the effects of various methods of treatment on the skin circulation of the toe and foot, as well as on the muscle and calf. These two areas should be clearly differentiated and should be studied independently, because decreases in the cutaneous circulation may result from exercise even though there is evidence of increased circulation through muscles.

Summary

Studies of the circulation of the toes, foot, ankle, and calf have been made before and after exercise in normal subjects and in patients with arteriosclerotic obliterative disease. The findings indicate that in the presence of arterial disease increased circulation through the exercising calf diverts blood from ankle, foot, and toe, resulting in relative ischemia of the toe during the postexercise period. An exercise tolerance test for the study of arterial insufficiency of the lower extremities is described.

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DISCUSSION

Dr. David I. Abramson, Chicago: First, I should like to ask Dr. Winsor whether the intrinsic muscles of the toes were involved in the exercise. Second, I should like to point out that the data presented by him are further evidence for a view which I have held for some time, namely, that sympathectomy has no significant effect upon blood flow in the muscles and therefore should not be used for the treatment of intermittent claudication.

Dr. Travis Winsor, Los Angeles: A sympathectomy has many uses but does not increase walking ability significantly. As to the question regarding the part being exercised, actually the calf muscle was being exercised, but the measurement of blood flow was being made at the toe. Thus, we were observing a circulatory change in the skin (toe) which was occurring because of the muscular activity of the calf. It appears that the calf muscle tends to divert blood from the skin to the muscle. In the presence of disease, when inflow is limited, the demands for blood in muscle are so great that there is not enough blood to supply the ankle, foot, and toes. Under normal circumstances the flow is sufficient to supply not only the muscle which requires added blood during exercise but to nourish the skin of the ankle, foot, and toe as well.

Simple Automatic Method of Blood Volume Control During Cardiac Bypass for Open Heart Surgery

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While evaluating the potential advantages of gravity drainage of the cavae, as compared with those of a venous pump, we found that verbal recommendations regarding the desirable distance between the right atrium and the blood level in the venous reservoir varied from 5 to 80 cm. H_2O. In plotting the relation of the caval drainage pressure gradient to the venous pressure in animals, we found that the curves had the same slope with varying flow rates and catheter sizes, and that they finally leveled off when the drainage gradient was less than 10 cm. H_2O. Since all of the curves were parallel, it seemed apparent that the slopes were dependent upon the outflow pressure and resistance characteristics, primarily, since the size and length of the connecting tubing remained constant. When the caval catheters were nearly as large as the dog's cavae, the venous pressure could be maintained below 10 cm. H_2O without lowering the venous reservoir very far below the cavae (e. g., 15 to 20 cm. H_2O). We also observed that the level in the oxygenator case remained remarkably constant when the venous pressure was below 10 cm. H_2O, but that this constant level was somewhat different at the different perfusion rates employed in plotting curves for each catheter size. This led us to investigate the relationship between various perfusion rates and the accompanying blood volume changes, and ultimately this led to the development of a method of automatic blood volume control which has appeared to be quite reliable and has simplified the management of clinical perfusions. The experimental observations have been described previously,[1] and may be briefly summarized as follows:

1. When the venous pressure was maintained below 10 cm. H_2O, as it was during this experiment and all other experiments described below, the amount of blood within the animal increased as the perfusion rate was increased. This was the result of an automatic shift of an equal quantity of blood from the extracorporeal to the intracorporeal portion of the perfusion circuit.

2. There appeared to be a characteristic blood volume for a given perfusion rate during an entire experiment in each animal, as evidenced by a return of the intra- and extracorporeal volumes to the original levels, even after stabilization at other levels associated with both slower and faster perfusion rates had been observed.

3. Stability of the animal's blood volume when the perfusion rate was kept constant was further tested by removing measured quantities of blood from a femoral artery or transfusing measured quantities into a femoral vein. It was not possible to de-

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Presented at the Sixth Scientific Meeting of the North American Chapter of the International Cardiovascular Society, San Francisco, June 21, 1958.

Now at St. Vincent's Hospital, New York (Dr. Gianelli). Research Fellow, Heart Association of Southeastern Pennsylvania (Dr. McMichael). Research Fellow, U. S. Public Health Service (Dr. McCaughan).

crease or increase the animal's blood volume by bleeding or transfusing in this manner, because an automatic, compensatory shift of almost exactly the same amount of blood into or out of the extracorporeal circuit occurred promptly. This relative constancy of the blood volume at a given perfusion rate, in spite of deliberate attempts to increase or decrease it by transfusion or "hemorrhage," appeared to provide a reasonable basis for control of the blood volume in patients undergoing open heart surgery with the aid of total cardiopulmonary bypass. We have now used this method in more than 30 patients and have found it to be reliable, within certain limits, which are discussed below.

Technique of Clinical Application

The conditions which seemed essential for successful clinical application of this method were maintenance of a low venous pressure (less than 10 cm. H_2O) and a constant arterial perfusion at a rate approximately equal to the patient's resting cardiac output. Caval catheters approximately three-fourths the diameter of the cavae, or larger, were chosen, and with this size the outflow resistance was lowered sufficiently to permit maintenance of a venous pressure below 10 cm. H_2O on bypass, in most instances, with the venous reservoir blood level less than 30 cm. below the cavae. The catheters were inserted just before the perfusion was started so that the period of partial obstruction caused by these large catheters could be minimized.

The period of partial bypass at the beginning and end of the perfusion was kept as short as possible because the experimental observations summarized above were made during total cardiopulmonary bypass, and significant alterations in blood distribution might occur if an unknown amount of blood passed through the heart for a considerable period of time. The period of partial bypass was usually less than a minute, both before and after total bypass.

The Kay-Gaertner modification of the Gibbon type of vertical screen oxygenator * was used in all these clinical perfusions. Blood was introduced into the apparatus, and the screens were filmed a short time before insertion of the cannulae into the patient was completed. Two or three pints of blood was added to the priming reservoir, in addition to the blood needed to fill the extracorporeal circuit. Replacement of blood lost while the chest was being opened and maintenance of a normal blood pressure prior to perfusion seemed important in achieving the most accurate blood volume control, presumably because this ensured optimal reflex responses and minimal changes in the patient's blood volume as perfusion was begun.

Simple application of the principles which appeared valid in the animal experiments seemed to be adequate in most patients. When the perfusion was begun, the arterial pump was quickly turned up to an estimated flow rate of about 2.2 L./sq.m/min., and the caval tapes were tightened after a short period of partial bypass, during which it was ascertained that the entire circuit was functioning smoothly. The level in the oxygenator case was marked as partial bypass was begun (Mark I), and after about two minutes on total bypass, which was permitted for stabilization, the level in the oxygenator case was again marked (Mark II). This was considered the level essential to maintain during total bypass. The level tended to fall, and this was due to automatic replacement of the blood volume of the patient as blood was continually lost from oozing surfaces, spilling over from the cardiotomy incision, etc. Blood was permitted to enter the oxygenator case from the priming reservoir fast enough to keep the level just below Mark II. Determination of blood loss by totaling the amounts weighed on sponges and in the suction bottles at frequent intervals during bypass was not necessary, since adequate replacement was automatically

* Manufactured by the Mark Company, Randolph, Mass.

taking place. At the end of total bypass, the level in the oxygenator case was brought back to Mark II by final release of an adequate amount of blood from the priming reservior, and the perfusion was then discontinued after a brief period of partial bypass. The caval drainage tube was partially occluded, if necessary, to return the level to Mark I.

After gaining confidence in this method, no attempt was made to measure blood loss during bypass in any way that would separate this period from the entire period of operation. The only figures used for calculating the blood balance for the entire operation was the amount of blood added to the oxygenator case from the priming reservior, and this was considered to be blood transfused into the patient.

A careful check on the blood loss at frequent intervals during bypass was not discontinued, however, until we had satisfied ourselves of the accuracy of this method by comparing the measured blood loss during bypass with the amount transfused from the priming reservoir. The correlation appeared to be remarkably good in all instances in which there were adequate time and personnel to measure all blood lost with reasonably accuracy.

The close correlation between blood transfused from the priming reservoir and the measured blood loss often came as a surprise to observers not familiar with this method. For example, when the pump-oxygenator team reported at the end of bypass that the amount of blood transfused from the priming reservoir was 1,500 cc., this often seemed excessive, since blood collected on sponges, whether weighed or not, totaled considerably less, but more especially because blood which collected in the thoracic cavity was not removed during bypass and was hidden from view. When both sides of the chest were sucked out and the figure for total blood loss was available two or three minutes after stopping the perfusion, it became apparent that the patient had not received too large a transfusion but, rather, that blood replacement had been remarkably accurate.

Comment

When the operative procedure and the perfusion were not complicated by unexpected events of a catastrophic nature, this method of automatic blood volume control appeared to be reliable and accurate. The correlation between automatic blood volume replacement from the oxygenator case and the measured blood loss was so close that measurement of blood loss during the bypass period was not performed with any urgency, and as our confidence in the reliability of the correlation increased, there appeared to be no need to measure the bypass blood loss separately, except for confirmation of the accuracy of automatic blood replacement. In the face of catastrophic hemorrhage, however, such as occurred during aortic-arch replacement, and after technical accidents which led to an ineffective heart beat, and an unduly long perfusion, the correlation between blood replacement through the oxygenator with blood loss became difficult to evaluate because of repeated periods of partial perfusion, slowing of the perfusion rate on total bypass due to lack of enough blood, etc. In addition, levarterenol U. S. P. (Levophed) appeared to contract the size of the vascular tree, as expected, forcing blood into the extracorporeal circuit and profoundly altering the reflex mechanisms responsible for automatic blood volume control. It seems unlikely that any other system of blood volume control, including the use of leveling devices to maintain a constant volume in the extracorporeal circuit, would have been much more helpful under such circumstances. When major hemorrhage occurs, it may be impossible at the end of bypass to evaluate the patient's blood volume or to guess with any degree of accuracy what his blood volume should be, as is well known to those who have been through such experiences.

We do not wish to present this method without a word of caution about the possible limitations, which have not been clarified at

the present stage of our studies. In particular, we have reservations about the total length of time for which the relationship of low venous pressure, constant perfusion rate, and constant blood volume may hold true. Recent experiments have suggested that after 30 minutes there may be a tendency toward the transference of more blood from the oxygenator to the patient than can be accounted for on the basis of blood loss. Whether this is due to transudation into the extravascular tissues, to progressive enlargement of the size of the vascular tree resulting from reflex changes, or to still other factors, such as evaporation, is not clear at present. Further studies will be necessary before definite statements can be made concerning perfusions lasting more than 30 minutes. This does not alter the fact, however, that this method has appeared to be reliable and accurate, both in animals and in patients, for total cardiopulmonary bypass at normal perfusion rates up to 30 minutes. The apparent tendency toward increasing the blood volume of the intracorporeal circuit after 30 minutes may well be to the advantage of the patient, at least as contrasted with the opposite tendency, i. e., undertransfusion. After 30 minutes the arterial blood pressure has remained normal or has increased, in the limited number of observations available at present.

Summary

Experimental and clinical experiences with a simple, automatic method of blood volume control during total cardiopulmonary bypass are described. Calculation of the blood balance has been much simpler when this method has been successfully employed. Accuracy of blood replacement, as well as simplicity of application, are the principal advantages.

University of Pennsylvania Hospital, 36th and Spruce Sts. (4).

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DISCUSSION

DR. ORMAND C. JULIAN, Chicago: It is important that all aspects of perfusion rate and maintenance of steady circulating blood volume in patients undergoing cardiac bypass be studied.

We are studying in our laboratory a perfusion factor which may have considerable effect on the method of blood volume control presented by Dr. Kirby. We have been able to show its effect on perfusion rate requirements.

The factor of peripheral resistance in the perfused animal can be studied by changing it during perfusion, using powerful vasodilators and vasoconstrictors. In one series of experiments we have observed a prompt deterioration of the electroencephalographic tracing when trimethaphan (Arfonad) is administered to an animal receiving an adequate and constant perfusion volume. This is accompanied by a marked rise in venous oxygen tension, lowered arteriovenous oxygen difference, and a fall in the extracorporeal reservoir chambers.

We are studying the part which may be played by peripheral resistance in the adequacy of calculated perfusion rates. The changes in blood volume of the patient indicated by reservoir changes probably should not be corrected unless the peripheral resistance is restored to normal.

These considerations may affect the application of the method reported by the authors.

DR. CHARLES K. KIRBY, Philadelphia: Dr. Julian has put his finger on a very important point. There is no doubt that this relationship is completely upset when you contract the size of the blood volume considerably with levarterenol (Levophed). We have made some studies, too, on the relation between peripheral resistance and low venous pressure at various perfusion rates. (Slide) Some investigators have found both in patients and in animals that there is a directly proportionate relationship between perfusion rate and mean arterial pressure. This certainly has not been the case in our experience. Here (slide) we have mean arterial pressure plotted as a function of flow rate; as you see, in going from 20 to 160 cc. the curves flatten off a great deal. Calculating the total peripheral resistance is not as easy as one might think. In order to calculate this, one has to use one of the variables which enter into the equation; i. e., one has to use variable A-V pressure differences; and, although a calculation does show decreased peripheral resistance using these figures, it is very questionable whether such data are reliable. As far as we can tell at this stage of the game, there is not sufficient change in peripheral resistance to upset the reflex relationships described during a period of 30 minutes, provided the patient does not undergo some catastrophic accident in which it is necessary to "upset the apple cart" by using levarterenol or some other vasoconstrictor.

Ectopia Cordis in a Twin

ELLIOTT S. HURWITT, M.D., and ALVIN LEBENDIGER, M.D., New York

Among the rarest, and at times the most spectacular, of congenital anomalies, ectopia cordis varies widely in its anatomical manifestations. The earliest report is apparently that of Niels Stensen in 1671, describing a cardiac monster with the heart and other organs protruding from the chest.[30] The unusual spectacle presented by an exposed heart beating on the chest wall in the unique setting provided by an apparently normal, probably identical, twin, prompted us to prepare a documentary film, showing the twins shortly after birth,* the surgical attempt to cover the heart, and the autopsy findings.† Approximately 150 cases of ectopia cordis have been reported, and the literature has been adequately reviewed by Greig, in 1926[7]; Roth, in 1939[23]; Blatt and Zeldes, in 1942[1]; Byron, in 1948[3]; Friedlieb and McDonald, in 1950,[6] and Major, in 1953.[17]

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From the Surgical and Laboratory Divisions, the Montefiore Hospital.

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Presented at the Sixth Scientific Meeting of the North American Chapter of the International Cardiovascular Society, San Francisco, June 21, 1958.

* The sequence demonstrating the twins together was furnished by Mr. George Silas, of Spring Valley General Hospital, Spring Valley, N. Y.

† The motion picture of the operation and autopsy was taken by Mr. Antol Herskovitz, medical photographer, Montefiore Hospital.

Report of a Case

The patient, the elder of twin boys, was born at Spring Valley General Hospital at 7:46 a.m. on Jan. 21, 1957, after approximately a seven-month gestation. The younger twin was apparently normal and vigorous for his size. The mother was a 34-year-old white woman, with an entirely irregular menstrual history, married for nine years, with no living children. There was a positive history of twins on both sides of the father's parentage. On the patient's arrival at Montefiore Hospital, the body temperature was 94 F. There was slight cyanosis, and obvious prematurity and immaturity. A large defect of the anterior chest wall extended from the base of the neck down to, and including, the umbilicus. The sternum was

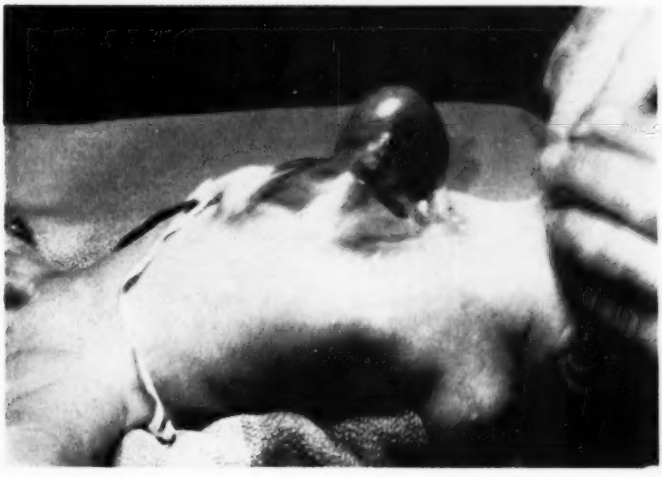


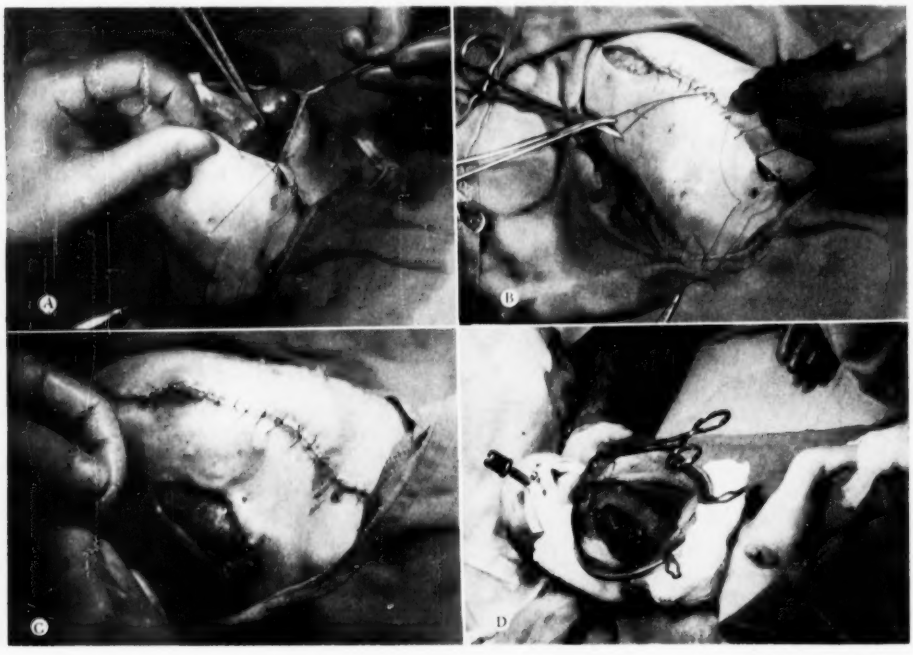
Fig. 1.—Photograph of heart projecting from chest wall, preoperatively.

completely unfused, and through the defect the heart projected, with its apex directed at a right angle to the body. A small appendage projected from each side of the heart close to the base. A large tubular structure extended superoposteriorly from the base, presumably representing the aorta and pulmonary artery. The heart suggested a three-chambered organ. The pericardium was absent. The lower part of the defect up to the heart was covered by peritoneum, with the liver beneath it, and the rectus abdominis muscles in the epigastrium were widely separated (Fig. 1). Asystole and respiratory arrest occurred several times, requiring cardiac massage and endotracheal intubation. Spontaneous respirations and heartbeat were reestablished on each occasion. Despite the apparently hopeless outlook, an attempt to cover the heart was decided upon.

At operation, the skin was mobilized around the entire defect, with vertical extensions superiorly to the root of the neck and inferiorly to the suprapubic area. Skin flaps were mobilized laterally to the flanks and axillae, allowing closure over the heart. Although the closure was not under undue tension, the heart rate slowed and became feeble. This occurred after any maneuver that changed the direction of the apex of the heart, however slight. In order to provide a covering for the heart and still leave the apex directed vertically, relaxing incisions were made in both midaxillary lines and the skin closed loosely over the apex of the heart. A residual defect in the right relaxing incision was covered with nonreactive cellophane, sutured to the skin edges. To prevent any change in the orientation of the heart caused by the weight of the skin flaps, traction sutures were placed in the flaps and tied to a tea strainer, which, in turn, was anchored to the top of the Isolette by a towel clip (Fig. 2). No anesthesia was used. A 25 cc. blood transfusion was given during surgery. Shortly after operation spontaneous respirations ceased. Endotracheal intubation and oxygenation with a respirator was instituted. Cardiac action became progressively feebler, and the infant died at 7:10 p. m. on Jan. 21.

At autopsy the infant weighed 1,950 gm. and measured 16 in. in length. The surgical wound, the external configuration of the heart, and the defect in the thorax and upper abdomen were as described above. The unfused halves of the sternum lay in the nipple lines. The clavicles were similarly defective. The pericardium was absent. From the umbilicus, an umbilical vein passed anteriorly over the liver and entered the right auricle. Bilateral superior venae cavae were present, the right emptying into the right auricle and the left into the left auricle (Fig. 3*A* and *B*). The inferior vena cava coursed posteriorly over the dome of the

Fig. 2.—*A*, *B*, *C*, and *D*, photographs of stages in providing a covering of skin for the heart, with lateral relaxing incisions and traction to minimize cardiac compression.



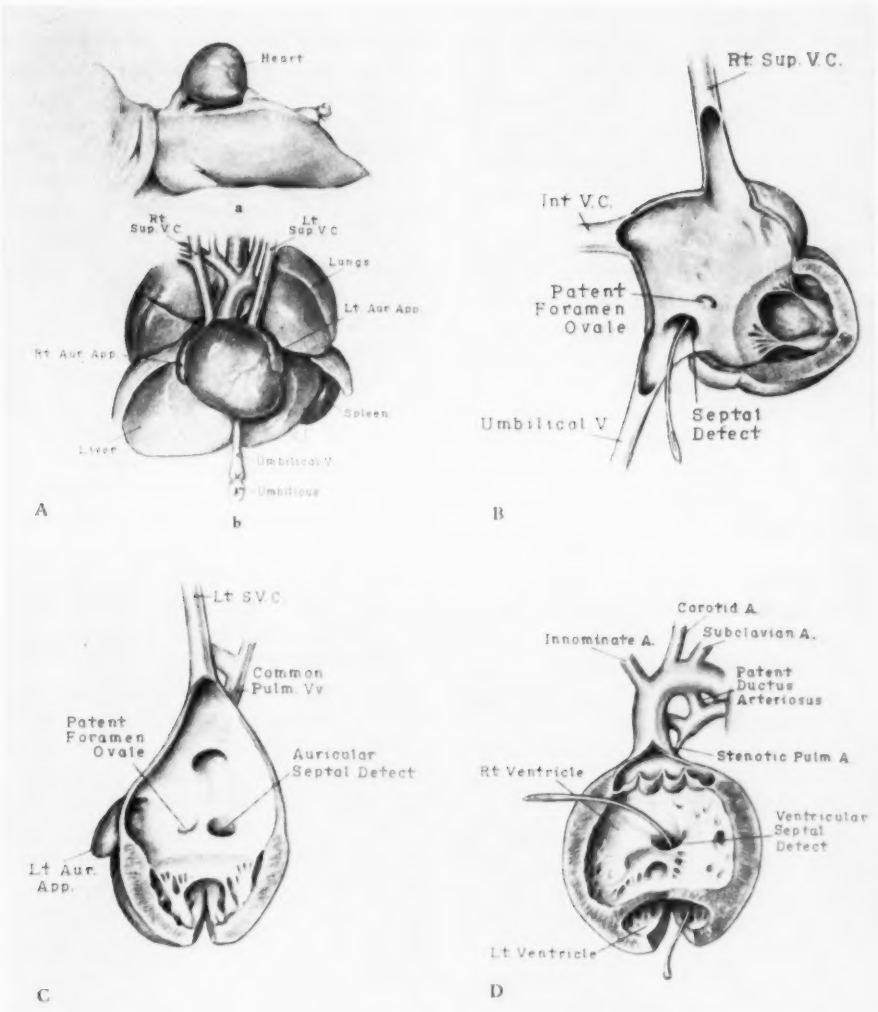


Fig. 3.—*A*, *B*, *C*, and *D*, diagrams demonstrating the multiple cardiovascular anomalies associated with ectopia cordis.

liver to enter the right auricle. A large auricular septal defect and a minute foramen ovale were present. The right ventricle dominated the heart, being hypertrophied and dilated. The outflow tract of the right ventricle was the aorta. A large patent ductus arteriosus was present. The common pulmonary artery was atretic, being represented only by a fibrous band, from the juncture of the right and left pulmonary arteries to the base of the right ventricle close to the aorta. Right and left pulmonary veins joined to form a common pulmonary vein, which entered the left auricle. The left ventricle was hypoplastic and emptied into the right ventricle through a large ventricular septal defect (Fig. 3*C* and *D*). Other abnormal findings consisted of a small cleft of the soft palate and bilateral undescended testes. On microscopic examination, congestion, focal hemorrhages, and inflammatory exudate were seen in the epicardium and endocardium. A fibrinous exudate covered the greatly thickened epicardium. The findings on the remaining sections were compatible with prematurity and the neonatal state.

At 4 months of age, the patient's twin was apparently normal and well developed,

having almost tripled his birth weight of 4 lb. 6 oz. (1,984 gm.). His growth pattern was also normal at one year.

Comment

In 1818, Weese[29] classified the available cases of ectopic cordis into three groups: cervical, thoracic, and abdominal. Byron added a forth: thoracoabdominal.[3] Survival, obviously, depends upon the nature of the ectopia and the variable presence of associated anomalies. The prognosis in the cervical type is extremely poor.[7] Laliberté, however, described an adult with the heart located in the neck and upper thorax.[11] In the thoracic type, the longest survival in Greig's collection was 13 months. Abdominal ectopia per se apparently is compatible with life. Deschamps reported his autopsy of an old soldier with suppurative nephritis of the right kidney and agenesis of the left kidney, with the heart occupying the left flank in lieu of the kidney.[4] Ramire described a 75-year-old man with an abdominal heart.[21] Survivals are common in the thoracoabdominal type, and it is in this group that late deaths are sometimes related to progressive constriction of the heart by the edge of the diaphragmatic defect.[17]

An early surgical repair is that of Lannelongue, in 1877, who sucessfully covered, by autoplasty, the heart of a 12-day-old girl and followed the patient for 20 years.[12] Attempts at surgical correction of this malformation have appeared with increasing frequency. The survivals have been confined to relatively minor degrees of the anomaly. Burton, in 1947, reported two patients with partial ectopia cordis, successfully covered with skin and costal-cartilage autografts.[2] Major described closure of a diaphragmatic defect and construction of a skin covering for the heart in an otherwise normal newborn infant with about one-third of the heart above the level of the thoracic cage, with survival.[17] This article also mentions an unreported success by Ravitch, who covered the heart with rectus muscle and fascia lata in an adolescent previously operated on for the tetralogy of Fallot.[22] In 1955 Scott described a successful repair of a partial thoracoabdominal defect in a 3-year-old child, performed by Brock in 1950.[25] A motion picture was shown by Lynn at the 1954 Annual Congress of the American College of Surgeons presenting the repair of a moderate defect in a newborn infant; the baby died several months later of pertussis.[13] Sabiston has recently reported a successful repair, the costal cartilages being transected to reinforce the closure.[24] In none of the survivals was the ectopia total, and in all the pericardium was intact.

In evaluating the surgical problem presented by ectopia cordis, it is necessary to accept the high incidence of associated anomalies that are incompatible with prolonged survival, such as bilocular and trilocular hearts, pulmonary atresia, tetralogy of Fallot, and septal defects. It is interesting to note, in this connection, that 6 of Greig's 38 cases had bilateral superior venae cavae, as in the case presented here.

The attempt at repair must take cognizance of the long-term implications of the deformity. Hence, if possible, diaphragmatic defects should be repaired if the heart will tolerate a change in its position. Correction of cleft sternum should be undertaken early, as the size of the cleft and the difficulty of repair apparently increase in a relatively short time. A defect in the sternum that could have readily been closed at birth required some tension when repair was performed seven weeks later.[16] Of course, the difficulties increase as the displacement of the heart from the mediastinum increases. The surgical successes to date have been limited to the thoracoabdominal type, thoracic ectopia cordis with minimal protrusion of the heart through a small defect or cleft in the sternum, and sternal clefts without true ectopia cordis. The only hope for major displacements at present is that the heart, if exposed, can be given adequate skin coverage.

The occurrence of ectopia cordis in one of twins probably monozygotic (the genea-

Zygosity of Twins

Hair color:	Normal twin: medium dirty blonde Deceased twin: dark blonde						
Eye color:	Both blue						
Ear lobes:	Normal twin: free Deceased twin: attached						
Finger prints:	Taking technically not feasible						
Blood typing of family:		Rh_0	rh′	rh″	M	N	P
Father	A	+	−	+	+	−	−
Mother	O	+	−	+	+	−	+
Normal	A	+	−	+	+	−	+
Deceased	A	+	−	+	+	−	+

Placenta: Described as being in one piece, with two separate sacs noted.

Absolute probability of the pair being monozygotic (per method of Smith and Penrose (*Ann. Human Genet.* 19: 273-289, 1954-1955) calculated as 77.54%; absolute probability of their being dizygotic, 22.46%. In other words, one cannot establish zygosity from data at hand.

logical data are contained in the accompanying Table) is indeed a rare phenomenon. Torkomian, in 1922, described a 3-year-old boy of a dizygotic twinship (the elder twin was female) with an incomplete sternum and thin, transparent skin overlying the defect.[27] Klassen mentioned his repair of a cleft sternum with protrusion of the pericardium in a 4-hour-old infant, although no details of the nature of the twinship are available.[10]

It is interesting that if, indeed, the patient was one of monozygotic twins, this has little, if any, bearing on speculation as to the etiology of ectopia cordis. The weight of evidence of well-documented cases has overturned the dictum of MacFarland and Meade, who stated, after an exhaustive review of the literature, that "one of homologous twins [does not] ever suffer from malformation not shared by its fellow."[14] In a painstaking study of 150 cases of twins with one twin blighted, Kindred found that blighting occurs with the same frequency in monochorial and in dichorial twins.[9] He felt that blighting probably represented an instance of purely environmental factors acting selectively on one embryo.

Stadler reported the case of a 7-year-old twin with tetralogy of Fallot and a normal twin similar in appearance and blood type.[26] Wade reported a case of pulmonary stenosis in one of probably monozygotic twins.[28] Forsyth and Uchida reported an auricular septal defect in one of identical twins.[5] Morison reported two sets of monochorial twins in which one twin was normal and the other grossly malformed.[18] As regards maternal infectious diseases, and their effect on the fetus, Penrose describes twins, one of whom had all the stigmata of congenital syphilis, the other having no such signs and a negative Wassermann reaction.[20] Occasional cases of patent ductus arteriosus in one of twins have been published.[15,28] However, the work of Kennedy suggests that postnatal factors may play a role in preventing closure of the ductus.[8] Congenital heart disease involving one of twins, with a normal sibling, has been encountered in four additional instances at the Montefiore Hospital. Successful repairs of an auricular septal defect, coarctation of the aorta, and a patent ductus arteriosus were performed in three of these situations. Fibroelastosis resulted fatally in a newborn infant in the fourth instance. Data available are inadequate to determine zygosity. In a report of a case of congenital cyanotic heart disease which he felt probably represented pseudo truncus arteriosus with collateral circulation to the lungs in one of monochorial twins, Paes, in 1956, stated: "At present there seems little doubt that, although it occurs rarely, intrauterine conditions can modify a genotypic pattern or permit the expression of a pathologic gene."[19] Whatever the etiologic factors are in the various forms of congenital heart disease, the variety that has been reported in one of identical twins suggests strongly that these factors can be operative in close proximity to a twin who is unaffected by them. It must be remembered, however, that far more frequently both twins are affected.

Summary

1. A case of thoracic ectopia cordis in one of twins is presented.

2. The problems associated with attempted surgical correction of the anomaly are described.

3. A motion picture is available of the twins together, the operation, and the autopsy findings.

Lucille J. Ross, M.D., of the Department of Health of the City of New York, obtained and made available the data in the Table.

Montefiore Hospital, 210 St. & Bainbridge Ave. (67).

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DISCUSSION

DR. HARRIS B. SHUMACKER, Indianapolis: I am sure that those of us who have encountered this rare difficulty have been plagued with the same problems as Dr. Hurwitt, namely, the difficulty of maintaining good contraction and the multiple congenital anomalies.

Congenital Coronary Arteriovenous Aneurysm

Clinical, Angiocardiographic, and Physiologic Findings on Three Patients with Successful Surgical Correction

B. M. GASUL, M.D.; E. H. FELL, M.D.; M. MOREANO, M.D., and M. WEINBERG JR., M.D., Chicago

Congenital coronary arteriovenous aneurysm with anomalous drainage into the coronary sinus, the right atrium, the right ventricle, or the pulmonary artery is a rare malformation. The authors found 16 cases reported in the literature, 6 of which occurred in patients under 16 years of age. Of these 16 patients, 3 with a preoperative diagnosis of patent ductus arteriosus were successfully operated on. One of these three patients was operated on at Cook County Hospital, and the case was reported in *The Journal*.[1]

We wish to report an additional three cases with an aneurysmally dilated right coronary artery draining into the right ventricle.

Report of Cases

CASE 1.—The case of a noncyanotic 7-month-old male infant was diagnosed clinically as one of arteriovenous coronary aneurysm. This diagnosis was confirmed by venous angiocardiography and cardiac catheterization. Corrective surgery was successfully accomplished.

CASE 2.—The case of a 5-year-old boy was diagnosed as one of congenital rupture of the right sinus of Valsalva on the basis of clinical, retrograde aortographic, and cardiac catheterization findings. At operation, this diagnosis was shown to be incorrect and an aneurysmally dilated right coronary artery which entered the right ventricle was successfully ligated and the aneurysm resected.

CASE 3.—A white boy, 9 years of age, whose case was diagnosed by us three years ago as one of congenital rupture of the right sinus of Valsalva on the basis of clinical findings, venous angiocardiography, retrograde aortography, and cardiac catheterization, was restudied recently. Because of our experience with Case 2 our diagnosis was changed to aneurysm of the right coronary artery draining into the right ventricle. This diagnosis was verified at operation, and a successful corrective procedure was accomplished.

Conclusion

We believe that we have established that the correct preoperative diagnosis can now be made on patients with these malformations by correlating the clinical and angiocardiographic findings, and that corrective surgery is feasible for these patients.

Cook County Children's Hospital, 700 S. Wood St. (12).

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DISCUSSION

DR. ISRAEL STEINBERG, New York: The four cases of coronary arteriovenous fistula reported by Dr. Fell and his colleagues constitute a world's record—no other group has had the opportunity of studying and operating in so many cases. Our review, cited by the authors, consisted of a single case diagnosed by intravenous angiocardiography. In addition, the details of 13 autopsy-proved cases of coronary arteriovenous fistula and 8 cases in which the diagnosis was established by exploratory thoracotomy were reported in order to establish criteria for diagnosis and treatment.

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Presented at the Sixth Scientific Meeting of the North American Chapter of the International Cardiovascular Society, San Francisco, June 21, 1958.

From the Pediatric Cardiophysiology Department of Cook County Children's Hospital, and the Hektoen Institute for Medical Research of Cook County Hospital, and the University of Illinois College of Medicine.

This is a brief resumé of our findings on the three patients. The complete paper with pertinent clinical, roentgenologic, electrocardiographic, angiocardiographic, and physiologic findings is now being prepared for future publication.

Our patient showed no evidence of disability over a seven-year period observation, and so we elected to continue observing her. Davison, McCracken, and McIlveen (*Brit. Heart J.* 17:569, 1955), however, reported the case of a 58-year-old woman with a coronary arteriovenous fistula who died of heart failure. Our study led us to conclude that surgical ligation of the artery or arteries carrying blood to a coronary arteriovenous fistula should be attempted if there was evidence of progessive cardiac disease. In a given case, however, surgery may be curative, or it may be impossible, depending upon the pathologic anatomy that is found at operation. All of the authors' patients were suitable for operation, and ligation of the arteriovenous channels may be expected to prevent heart failure and bacterial endocarditis.

While in Chicago a year ago, at the time of the American Heart Association meetings, Dr. Gasul showed me one of the retrograde studies and the beautiful demonstration of the coronary arteriovenous fistula that was shown here. There is no doubt that this method of angiography for coronary-artery visualization is superior to intravenous angiocardiography. However, it must be pointed out that aortic puncture is riskier than angiocardiography done intravenously.

DR. HARRIS B. SHUMACKER, Indianapolis: Thank you very much Dr. Steinberg. Is there any further discussion—Dr. Kittle?

DR. C. FREDERICK KITTLE, Kansas City, Kan.: I should like to compliment Dr. Fell on his fine presentation and mention another case of a slightly different anomaly involving the coronary artery.

Recently we operated on a 6-year-old boy with a loud, continuous murmur along the left sternal border, maximum at the second intercostal space. Fluoroscopy showed slight enlargement of the left ventricle, and left ventricular hypertrophy was noted on the electrocardiogram. The blood pressure was 106/70. At the time of operation no ductus arteriosus was found, but a branch from the left coronary circumflex artery was found to pass directly into the left atrium. This, then, was a fistula between the left coronary artery and the left atrium. By placing a clamp across the base of the left atrial appendage, the fistula was obliterated, and the thrill disappeared. The left atrial appendage was removed. This was a rather unusual instance of coronary arteriovenous fistula, since most of the previously reported cases have involved the right coronary artery.

DR. ADRIAN KANTROWITZ, Brooklyn: I, too, would like to add my applause for Dr. Fell and his group. I rise only to ask a question. As I understand it, Dr. Fell, the main right coronary artery was ligated in both Cases 3 and 4; this presumably, then, would eliminate the normal blood supply to the right ventricle by the right coronary artery. I should like to know whether there were any obvious communications from the left coronary artery to supply this arterial bed.

DR. LEWIS H. BOSHER JR., Richmond, Va.: We have seen a case, an operative one, which I think might have been of enough interest to justify our showing two or three slides.

(Slide) This patient was a 2½-year-old child who had been in repeated cardiac failure from the age of 4 months. She presented evidence of considerable cardiac hypertrophy and a very large pulmonary conus. There was a loud systolic murmur to the left of the sternum, with a Graham Steell murmur of pulmonary insufficiency. No other diastolic murmur was heard. The electrocardiogram showed right ventricular hypertrophy. This child had been studied one year before by cardiac catheterization, with interesting findings. There was an oxygen step-up in the pulmonary arteries, suggesting patent ductus or an aorto-pulmonary-septal defect. In addition, there was some oxygen step-up in the right atrium. A retrograde aortogram was obtained. Perhaps you can follow this better than we did at the time. We did not interpret it properly. A patient ductus was present. We thought also of a ruptured sinus of Valsalva or regurgitation through the pulmonary and tricuspid valves. You will see something coming off one of the coronary sinuses which is important in the operative findings.

(Slide) This patient was operated upon, and a very large ductus was found. There was severe pulmonary hypertension. The ductus was temperarily occluded, and thereafter it was divided. After the ductus was divided, we realized that there was still a trill over the right atrium. We had done the operation on this child through a transsternal excision, with the heart-lung machine available because of the possibility of an aneurysm of the sinus of Valsalva. We noticed, in addition, that there was a large aneurysmal dilatation of the left coronary artery, with a vessel coming off which passed through the transverse sinus (slide) and entered medially behind the superior vena cava into the dilated right atrium. This vessel was ligated at this point, without any change in the electrocardiogram. Unfortunately, this child died about 24 hours after operation, we believe from the effects relating to the pulmonary hypertension, rather than as a result of the division of the coronary vessel. At autopsy the lungs were found to be markedly congested.

DR. HARRIS B. SHUMACKER, Indianapolis: I should like to ask Dr. Fell a question. Wouldn't it be more accurate to describe these aneurysms as coronary artery-ventricular fistulae?

DR. E. H. FELL, Chicago: I believe your terminology is quite right, Dr. Shumacker. We do have an arterial venous flow from high-pressure

to low-pressure areas, or an arteriovenous fistula, between a coronary artery and the right ventricle.

I agree with Dr. Steinberg that most of these cases can be accurately diagnosed without retrograde aortography. However, in our retrograde aortograms recently, we have had very little trouble, using 50% diatrizoate (Hypaque) sodium, and having the end of the catheters right down in the ascending aorta. As you noted, they did visualize these anomalies very well. You also saw that the angiograms likewise show the anomalies. Dr. Kantrowitz questioned the indications for surgery, as did Dr. Steinberg. How do we dare tie off these coronaries? I believe that in all these cases the anomalous coronary vessels with fistulae are really very harmful to the child, like any other arteriovenous fistula. A collateral circulation has been established that provides blood to the myocardium. The Thebesian vessels aid in the circulation.

Dr. Bosher's case is indeed most interesting. In the literature is found the case of the left coronary artery passing through the left atrium and then inserting into the right atrium. I believe there is one other case, and I refer again to the very excellent review of the literature by Dr. Steinberg and associates.

Massive Systemic-Pulmonary Arterial Shunt Through Multiple Pleural Adhesions

PAUL T. DE CAMP, M.D., and HURST B. HATCH JR., M.D., New Orleans

The following case presents well-documented evidence of a massive systemic-pulmonary arterial shunt occurring through multiple arterialized adhesions between the wall of the chest and the upper lobe of the left lung. Severe symptoms suggestive of systemic vascular insufficiency and evidence of the shunt disappeared after freeing of the pleuropulmonary adhesions. In all these respects this case is, to our knowledge, unique.

Report of a Case

A white woman, 34 years old, was admitted to the Ochsner Clinic on Aug. 29, 1956, complaining of "weak spells" of 18 months' duration. In February, 1955, she awoke choking and gasping, and her breathing was rapid and shallow. She was unconscious for 10 minutes, and, on regaining consciousness she felt numb all over. Similar attacks recurred initially at long intervals and then more frequently. In the preceding five months she had had five major attacks, the last occurring 10 days before admission. Subsequent spells were accompanied by numbness from the left elbow to the shoulder and localized pain in the left side of the chest. The pain had persisted since the last attack. The attacks were frequently followed by right-sided throbbing headaches. Skipped heart beats were common. At times the attacks followed increased activity, and the condition had seriously interfered with the patient's normal activities.

The patient had been suspected of having tuberculosis, but results of repeated sputum studies and skin tests had been negative. She had had no significant pulmonary symptoms until 1952, when acute dyspnea heralded acute spontaneous left pneumothorax. A needle was inserted to the left of the sternum for purposes of poudrage, but a quantity of blood was accidentally obtained and this, rather than powder, was reinjected to produce adhesions. She recovered and experienced no further symptoms until onset of the present illness.

On admission, the patient was 67 in. tall and weighed 108 lb. She had neither cyanosis nor clubbing. The pulse was regular, and the blood pressure was 106 mm. Hg systolic and 70 mm. Hg diastolic. A systolic murmur or souffle was heard over the upper left side of the thorax anteriorly and posteriorly. The lungs were resonant and free of rales. The pulmonary second sound was abnormally loud. A loud, long systolic murmur was heard over the base of the heart, being loudest in the left second and third interspaces. There was no thrill. The liver was not enlarged, and peripheral edema was absent.

Results of laboratory tests, which included blood count, sedimentation rate determination, urinalysis, fecal examination, fasting blood sugar and urea estimations, and Wassermann tests, were normal. Results of skin tests for blastomycosis, coccidioidomycosis, and histoplasmosis and with 1:1,000 old tuberculin U. S. P. were negative. Roentgenography of the chest revealed apparently old fibrotic lesion in both lungs in the region of the lateral portion of the first and second anterior interspaces (Fig. 1). The hilar shadows were slightly retracted superiorly. Nothing to suggest a pulmonary arteriovenous fistula was seen. The size and contour of the heart were normal except that the pulmonary conus was somewhat prominent. At fluoroscopy the pulsations appeared within normal limits. The electrocardiogram revealed normal sinus rhythm, vertical electrical position, high voltage of P-waves in Leads II, III, and aV_F, R-R^1 in Lead V_1, and a broad S-wave in Lead I. This was interpreted as showing atrial strain with some delayed activation of the right ventricle. A phonocardiogram over the third left interspace near the sternal border revealed a long systolic bruit with midsystolic accentuation (Fig. 2).

The patient was admitted to the Ochsner Foundation Hospital for further study. Cardiac catheterization revealed normal pressures through-

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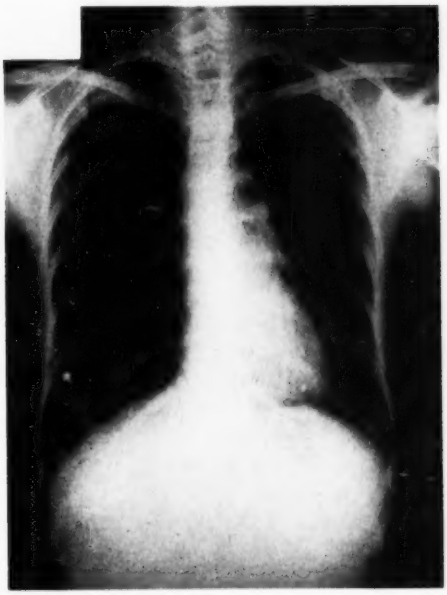

Fig. 1.—Preoperative roentgenogram of the chest shows old fibrotic lesions in both lungs in the region of the lateral portions of the first and second anterior interspaces.

out (Table). There were a rise of 1 vol. % in the oxygen content of the blood on entering the right atrium and a striking rise of almost 3 vol. % in the blood on entering the left pulmonary artery. The level of 15.2 vol. % in the left pulmonary artery was greater than the level in the brachial artery, which was 14.9 vol. %, and represented a 95.5% oxygen saturation. The systemic blood flow was estimated at 7.2 liters per minute, a great elevation. There was, therefore, evidence of a possible left-to-right shunt at the atrial level and of a certain massive one into the left pulmonary artery. The size of this shunt could not be estimated because the oxygen content of the blood in the pulmonary artery was higher than that in the brachial artery. The diagnosis of a systemic-pulmonary artery shunt was made, and the shunt was presumed to be the result of trauma to the vessels by the needle in 1952.

At operation, on Sept. 19, the superior 40% of the upper lobe of the lung, otherwise grossly normal, was seen to be densely adherent to the mediastinum and the wall of the chest. On lysis these adhesions contained myriads of pulsating blood vessels forcibly ejecting bright red blood. Control of bleeding was difficult, and 3,500 ml of whole blood was given. The left pulmonary and main pulmonary arteries were exposed from the hilus of the left lung to the right ventricle. Dissection all the way around both vessels failed to reveal any unusual systemic arterial communication. Samples of blood from the left pulmonary artery and the base of the main pulmonary artery were comparable in color. It was therefore reluctantly concluded that the systemic blood entering the left pulmonary artery came from the numerous minute arterial vessels traversing the pleural adhesions.

The preoperative loud, long systolic murmur was replaced postoperatively by a much less prominent systolic basal murmur. Multiple pre-

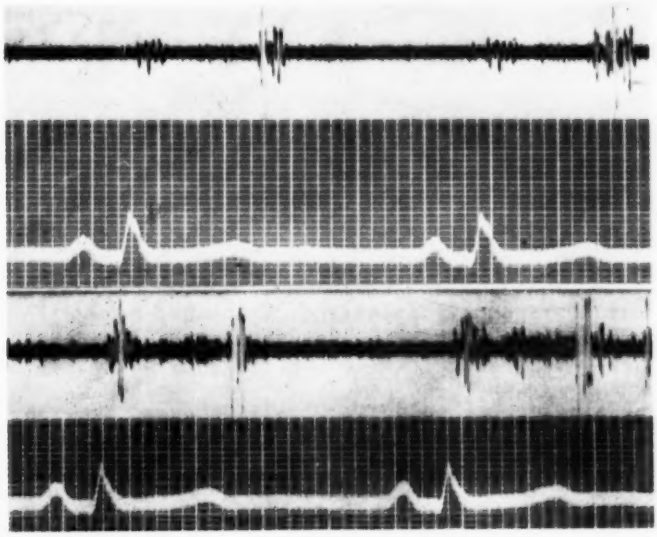

Fig. 2.—Phonocardiogram recorded over the left third interspace near the sternal border shows a long systolic bruit with midsystolic accentuation.

Data Obtained from Right-Heart Catheterization

Location	Oxygen Content, Vol. %: 9/12/56 Before Operation	3/28/57 After Operation
Pulmonary capillary	12.0	11.9
Right pulmonary artery	11.7	11.8
Left pulmonary artery	15.2	11.3
Main pulmonary artery	11.5	--
Right ventricle	11.1	10.6
	11.1	
Right auricle	11.5	11.9
	11.5	11.7
	11.4	10.9
Superior vena cava	10.2	11.0
	10.5	10.4
Brachial artery	14.9	
Femoral artery		14.8
Per cent saturation of arterial blood	95.5	96.1
Systemic blood flow (liters per minute)	7.2	4.1

All pressure determinations within normal limits

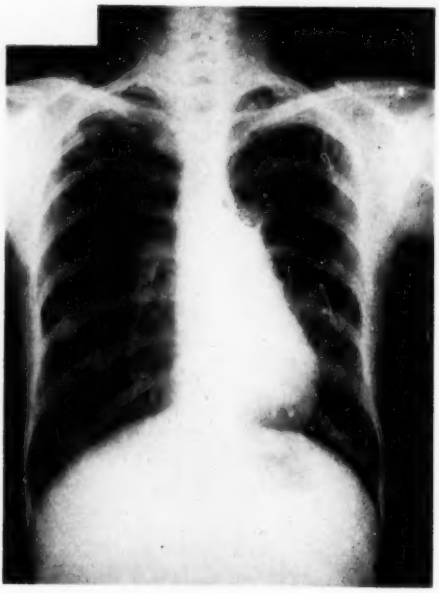

Fig. 3.—Postoperative roentgenogram of chest, made Aug. 14, 1957, is similar to the preoperative film except for the presence of retention wire sutures.

mature systoles appeared on the second postoperative day but disappeared three days after administration of quinidine. The patient was discharged from the hospital on the 11th postoperative day and returned to work on the 17th postoperative day.

When seen in January, March, and August, 1957, the patient reported complete relief of all preoperative symptoms. The systolic basal murmur became less prominent and finally inconstant. The postoperative roentgenogram was satisfactory (Fig. 3). Cardiac catheterization in March, 1957 (Table), demonstrated no rise in the oxygen content of the blood in the pulmonary arteries. The cardiac output was at a normal level of 4.1 liters per minute. In September, 1957, spontaneous right pneumothorax developed, but this resolved without aspiration. In June, 1958, the patient wrote that she was asymptomatic and working regularly.

The operative findings and response to freeing of the pleuropulmonary adhesions established a diagnosis of massive systemic-pulmonary arterial shunt occurring through multiple minute arterial vessels in the dense adhesions over the apical and posterior portions of the upper pulmonary lobe. These may have developed after the spontaneous pneumothorax and induced hemothorax in 1952.

Comment

Normally, the only systemic-pulmonary arterial communication is between the bronchial and the pulmonary arteries at the capillary or arteriolar level.[1-3] In human perfusion studies[4,5] alterations in the pressure in the bronchial artery led to changes in the pressure in the pulmonary artery and to pulmonary venous and azygos venous flows. There is no evidence of retrograde flow of arterialized blood into the pulmonary arteries. In congenital heart disease associated with reduced blood flow to the lungs a considerable increase in bronchial arterial blood flow commonly occurs.[5] Bronchial arteries have been observed to enlarge significantly in tuberculous and nontuberculous chronic pulmonary inflammatory disease,[5] in association with acquired mitral stenosis,[5] and in severe bronchiectasis.[6]

Anomalous communications between the systemic and the pulmonary arteries may be congenital. Persistence of the ductus arteriosus is the commonest. Less frequently a defect occurs in the aortic septum.[7-10] "Pulmonary sequestration" is regularly associated with one or more aberrant arteries arising from the aorta or its branches and

communicating with the pulmonary arteries within the sequestered lung.[11-16] Vessels from the aorta entering apparently normal lungs have been reported.[17] Cases of pulmonary arteriovenous fistulas have been described in which important systemic arterial communications have also been found to the affected area of the lung.[18,19]

Abnormal systemic-pulmonary arterial communications may also be acquired. They may result from penetrating injuries.[20-22] Numerous cases of rupture of aortic aneurysms into the pulmonary artery have been reported.[23,24] These may be syphilitic[24,25] or acquired aortic sinus aneurysms.[26] Recently, Davila and associates[27] reported a case in which, after arrest of blastomycosis of the lingula, signs of a vascular fistula in the area developed, with notching of the adjacent ribs. At operation heavily vascularized adhesions were found between the diseased lung and the overlying thoracic wall, communicating freely with large arterial vessels on both sides. Division of the adhesions and lingulectomy caused the signs of a fistula to disappear.

The case herein reported indicates that arterialized adhesions may develop between the parietes and the grossly normal lung, that the systemic-pulmonary arterial shunt may be sufficient to produce symptoms of cerebrovascular insufficiency, that such a shunt may be detected by right-heart catheterization, and that division of the adhesions may interrupt the abnormal shunt and relieve all related symptoms.

The question immediately arises as to the frequency and clinical significance of this condition. Vascularized pleuropulmonary adhesions are commonly found at thoracotomy, and in some instances a pulsatile flow occurs from divided vessels. Vigorous pulsatile flow must indicate a systemic arterial communication, and the direction of the blood flow must be from the thoracic wall into the lung. Our case indicates that a considerable quantity of such blood may flow back into the pulmonary artery. A systolic, or continuous, murmur or souffle is characteristic, and one recalls with quizzical interest the older clinicians' concern with souffles of extracardiac origin in cases of pulmonary tuberculosis![28]

It need hardly be mentioned that in all systemic-pulmonary arterial communications the shunt consists of recirculation of previously oxygenated blood through the lung. Unoxygenated venous blood does not pass into the arterial circuit unless severe pulmonary arterial hypertension has developed. Therefore, in cases of systemic-pulmonary arterial communication, cyanosis, clubbing, and reduced arterial oxygen saturation do not occur. Signs of the fistula will be limited to a systolic or continuous thrill or murmur and the radiologic evidence of notched adjacent ribs if intercostal arteries have sufficiently enlarged.[27] The shunt may significantly increase the myocardial work load, which is characteristically shared equally by the two ventricles. If enough blood is deviated from the normal systemic pathways, syncope and other symptoms of cerebrovascular insufficiency may develop.

Intravenous angiocardiography is not a useful diagnostic method unless recirculation of aortic blood into the pulmonary circuit can be demonstrated. The anomalous communication may be demonstrated by intra-aortic injection of dye, which is particularly useful in solitary vascular communications.[9] Catheterization of the right side of the heart is a particularly valuable diagnostic method,[16,25] as illustrated in our case. It will demonstrate clearly any fistulous communication giving rise to a significant left-to-right shunt, and will permit estimation of the cardiac output and some evaluation of the extent of the load placed on the circulation by the abnormal shunt.

Additional information as to the frequency and significance of acquired systemic-pulmonary arterial shunts associated with pleuropulmonary adhesions will not be obtained unless the condition is suspected and right-heart catheterization performed before operation. It is suggested that in all cases of possible pleuropulmonary ad-

hesions careful physical examination be performed with this condition in mind. Right-heart catheterization is recommended in cases in which a murmur or souffle suggests a fistulous communication, cases with unexplained rib notching, or cases of systemic vascular insufficiency due, possibly, to systemic-pulmonary arterial communication. In selected cases aortography may give additional information.

Summary

A case is reported in which a massive systemic-pulmonary arterial shunt occurred through pleuropulmonary adhesions to the left upper lobe of the lung. This shunt increased the resting cardiac output by 75% and produced repeated attacks of choking and syncope. Division of pleuropulmonary adhesions resulted in relief of all symptoms and eradicated the abnormal shunt. The possible considerable clinical significance of such shunts through pleuropulmonary adhesions is emphasized.

350 3 Prytania St. (15)

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Use of Atrial Grafts for the Closure of Cardiac Defects

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Surgical experience with open-heart procedures has shown that there are a variety of cardiac abnormalities which require some type of graft to repair the defect most satisfactorily.[3,4,7,10,11] While many of these defects can be closed by simple suture approximation, there remain many which require a patch or graft to correct the abnormality. A list of such defects would include atrial septal defects, atrioventricularis communis, ventricular septal defects, infundibular stenosis, and certain types of acquired cardiac lesions.[12] Possible applications for such grafts may arise in the surgical treatment of cardiac aneurysms and in selective reconstitution of the ventricular wall following myocardial infarction.

There have been several excellent investigative approaches to assess a variety of materials which might he used in the closure of such defects.[1,6,14] The types of materials used in such studies include homologous aorta, autologous and homologous pericardium, external jugular vein, plastic discs, rigid screw-on buttons, polyethylene, polyvinyl formalinized (Ivalon *) sponge, Ivalon wrapped in pericardium, and atrial grafts, both homologous and autogenous. Donald et al.[6] concluded that Ivalon was the best of the materials they used and that the plain Ivalon was the prosthesis material of choice, as it was readily permeated with connective tissue. Furthermore, there was no loosening of the prosthesis, and after healing there was less deformity of the atrium when this material was used to close artificially created interatrial septal defects. As a result of this study and a similar one by Bahnson,[1] Ivalon now is the most popularly accepted material used clinically for the closure of cardiac defects.

Watkins et al.,[14] among other materials, used homologous and autogenous atrial grafts to close experimental atrial defects, and, though they had no disruptions of the graft, they felt that the "infarctive necrosis" seen histologically in these grafts eliminated their prospects for clinical application. They observed, too, that homologous atrial grafts showed a slower rate of replacement than did autologous atrial grafts.

Because of several theoretical (and emotional) disadvantages to the use of plastics within the heart, a detailed study of the fate of autogenous atrial grafts used for closing cardiac defects was undertaken. The observations and results of this study, constitute the basis of this preliminary report.

Method

Thirty mongrel dogs were used for this study. The animals were anesthetized with intravenous thiopental (Pentothal) sodium, and, using a Jefferson positive-negative endotracheal respirator, either the right or the left thorax was entered through the third or fourth intercostal space. The pericardium was opened, and the right or left atrial appendage was amputated. In 12 animals the atrial appendage was resutured to the atrial wall,

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Fig. 1.—Right atrial view of free atrial-graft closure of atrial septal defect. Early thrombus formation on the endocardial surface of graft is noted.

from which it was excised. In these the Satinsky clamp was left in place until the atrial patch was reattached. In the remaining dogs the free full-thickness portion of the atrium was tailored and trimmed as necessary to close artificially created cardiac defects in the atrial septum, right ventricle, or opposite atrium. The grafts varied from 2 to 5 cm. in diameter. If the amputation site was not used as the site of the graft, it was approximated with a single continuous suture of 000 silk. For the creation and repair of atrial septal defects and ventricular defects, a heart-lung bypass system, utilizing a DeWall bubble oxygenator, was employed.[5] All the atrial grafts were secured by a single row of continuous 000 silk. The chest was closed in a routine manner, and intercostal catheters were used as required. The animals were then killed at various intervals. When each animal was killed, the ascending aorta was opened, and, under direct vision, the right and left main-stem coronary arteries were cannulated securely. Both coronary arteries were then injected with a Vinylite-lead mixture, as described by Kaplan,[6,8] after meticulous removal of the pericardium. The area of the heart in which the graft had been applied was removed with adjacent normal myocardium, and x-rays of this segment were obtained. Histological sections were then taken on each specimen, and standard hematoxylin-eosin and Masson trichrome stains were obtained.

Results

There were no disruptions of the autogenous atrial grafts in any of the dogs. The only death occurred within 24 hours in five animals following cardiac bypass and was due to postoperative hemorrhage, a sequence encountered by us before.[2] Twen-

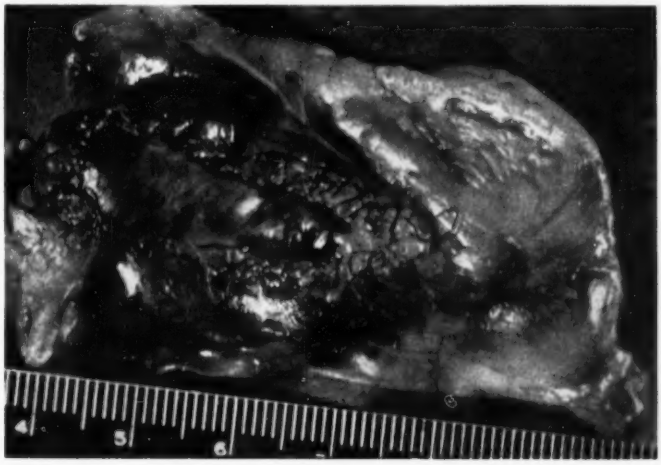

Fig. 2.—Atrial graft used for closure of defect in the atrial wall. The suture around the periphery of the graft can be seen. Graft is nine days old. The picture shows the external surface of the heart.

Fig. 3.—Same heart as in Figure 2, seen from the endocardial surface. The heavy thrombus formation overlying the graft is evident.

ty dogs were killed, and five dogs are alive and well. These are being followed for long-term studies and are now in the 6th to the 16th month after application of the graft.

Figure 1 shows an atrial graft which was used to close an artificially created atrial septal defect. This animal was killed two days after the graft insertion. In this photograph, taken from the right atrial side with the endocardial surface of the graft shown, early thrombosis about the graft is noted. The same phenomenon occurs on the opposite, or epicardial, surface of the graft, and within 14 to 21 days both surfaces are lined with an endothelial-like surface.

Figure 2 is a photograph of a full-thickness free atrial graft nine days after its application to a defect in the right atrial wall. The graft measures 4.75×1.5 cm. on the specimen. The epicardial surface of the heart is shown. The internal aspect of this same graft is shown in Figure 3. Thicker and more organized thrombosis is noted overlying the graft. In Figure 4 the microscopic section of this same graft is shown. It has been stained with the Masson trichrome technique. In the upper right aspect the heavy thrombus overlying the

Fig. 4.—Microscopic section of graft seen in Figures 2 and 3. The thrombus is seen in the upper right aspect of the graft. In the graft proper (lower half of photograph) necrotic muscle is seen. Viable fat cells, connective tissue, and some muscle remain.

Fig. 5.—External heart surface showing a 3-month-old atrial graft used to close an atrial defect. Arrows indicate the periphery of the graft.

Fig. 6.—Endocardial aspect of graft shown in Figure 5. The smooth endothelial lining of the graft is demonstrated. Arrows outline the graft.

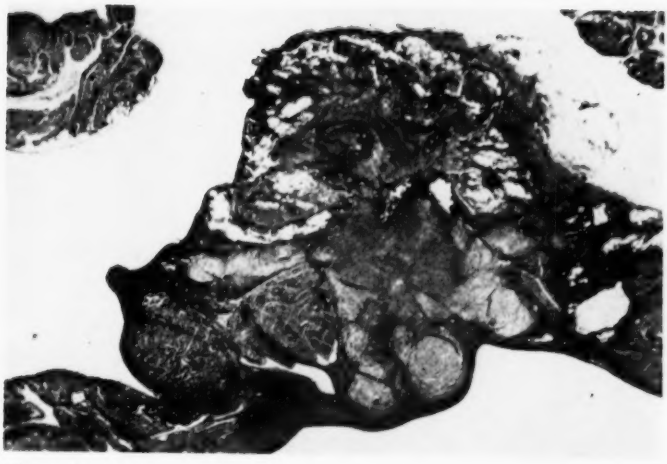

Fig. 7.—Photomicrograph of graft shown in Figures 5 and 6. In the right and left lower aspects of the photograph normal myocardium can be seen at the graft junctions. Between this is the graft, which is now a dense scar.

Figure 8

Fig. 8.—X-ray after injection of coronary arteries of heart shown in Figures 5, 6, and 7. Blood vessels can be seen readily in the graft itself. Discussion in text.

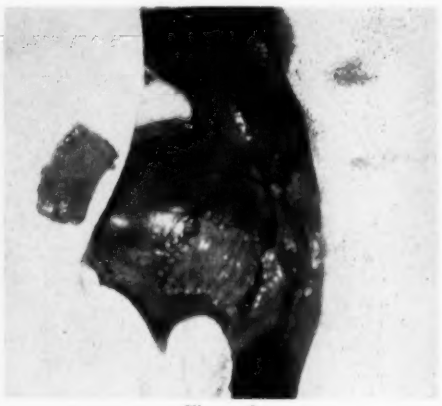

Figure 9

Fig. 9.—Full-thickness atrial graft on right ventricle wall. Discussion in text.

graft is seen. In the graft itself there appears to be some viable muscle along with necrotic muscle. The fat cells and the fibrous connective tissue appear viable, however. Histologically, then, there is evidence of viable connective tissue elements in the graft, although there is some loss of muscle in the graft itself at nine days.

Figure 5 shows the epicardial surface of a full-thickness atrial patch used to close a full-thickness defect in the right atrium after three months. Slight contraction of the graft has occurred. In Figure 6 the endocardial aspect of the same graft is shown; the heavy scarring is evident, and a smooth, normal-appearing endocardial surface covers the patched area. Figure 7 is the histological section of this same graft. In the lower right and left corners, normal muscle adjoining the graft can be seen. The central portion of the picture shows a thick, dense fibrous connective tissue scar. There are numerous blood vessels in the scar. Figure 8 shows the x-ray taken after injections of the coronary arteries and en bloc removal of the atrium. The closed loop of the wire

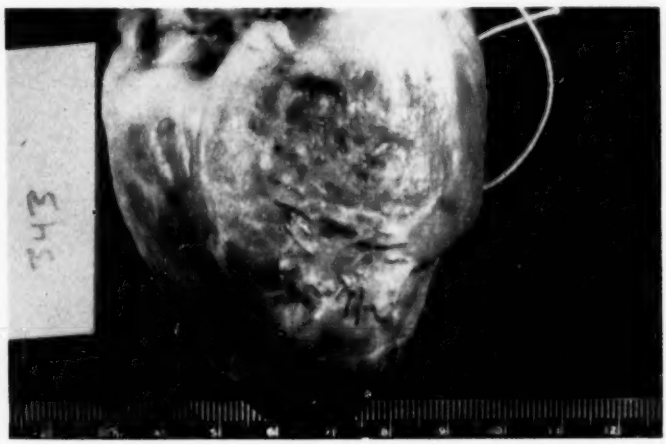

Fig. 10.—Heart shown in Figure 9, two months after grafting of right ventricular wall. The sutures along the periphery of the graft are shown.

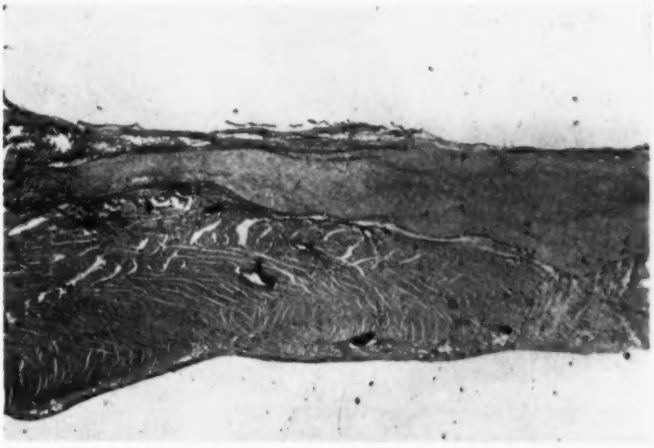

Fig. 11.—Photomicrograph of graft shown in Figure 10. The minimal reaction at the juncture of the graft (above) and the normal myocardium (below) can be noted.

(in hemostat) encircles the incision line of the graft. Blood vessels traversing the suture line into the graft are readily seen.

In Figure 9 a patch of full-thickness atrium is shown sutured in place onto the anterior surface of the right ventricle. A square window of myocardium of half-thickness was excised (on the towel at the bottom of the picture) and the graft sutured in its place with a continuous 000 silk suture. This photograph was taken at the time of operation. Figure 10 is a photograph of the same heart two months later. The pericardium has been removed. The sutures along the perimeter of the graft can be seen. Normal thickness of the right ventricular wall as the graft site was maintained, and the thickness of the graft was unchanged. Figure 11 shows the histological section of this graft. The thick, uniform fibrous tissue replacement of the atrial graft is well delineated from the underlying myocardium. There is virtually no reaction at the junction of the graft and heart muscle. In Figure 12 is an x-ray of the right ventricular wall and the overlay graft after injection of the coronary arteries, as described. It is an end-view of the heart wall after transection of the middle portion of the graft. The generous blood supply to the graft itself (top of specimen) is clearly demonstrated. Adhesive tape is holding the specimen in position.

Fig. 12.—X-ray after coronary injections of graft shown in Figure 10. Large vessels into the graft (upper aspect of specimen) are clearly demonstrated. A piece of adhesive tape is holding the specimen in position.

Comment

From this study to date, we conclude that free full-thickness atrial grafts used to close artificially created cardiac defects serve well to patch such holes. Furthermore, these autologous grafts remain viable after their placement. While there is gradual replacement of the myocardium, the fat cells and connective tissue in the grafts remain viable, while replacement of the muscle gradually occurs. These atrial grafts,

as has been shown, soon are traversed or invaded by blood vessels across the suture line from the normal myocardium. This phenomenon has been demonstrated as early as seven days after applying the graft. This suggests, therefore, that these grafts early acquired their own blood supply. When the muscle of a graft has been replaced by connective tissue, there results a firm, dense scar, which is stronger than normal myocardium. Necrosis and disruption of an atrial graft have never been observed during this study. Thrombosis formation occurs at the graft surface, and this surface is reendothelized by the third week. The same phenomenon occurs on both the epicardial and the endocardial surface of the graft. This same observation was reported by Watkins.[14]

The advantages of an atrial graft may be listed as follows: 1. It is readily available as autologous tissue from either atrial appendage.. 2. It is readily tailored and is handled with ease during its application. 3. It affords a living framework upon which connective tissue replacement of muscle may occur. 4. It acquires a generous blood supply of its own early after application. 5. It forms a very firm, tough patch, which is unlikely to undergo aneurysmal dilatation. 6. It, of course, produces no foreign-body reaction and leaves no foreign body in place.

Summary

The results of this study thus far suggest that the use of free full-thickness atrial graft is feasible for the repair of cardiac defects. The clinical application of such grafts has not been realized, but their use for such a purpose is contemplated after long-term studies on their fate is completed, in the near future.

Interpretation of the histological sections was made by Dr. Charles F. Begg.

St. Luke's Hospital, 421 W. 113th St. (25).

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DISCUSSION

DR. DENTON A. COOLEY, Houston, Texas: I have been interested in finding the most satisfactory patch for ventricular septal defects, since I believe a large number of such lesions do not lend themselves to direct surgical suture. Avoidance of tension is important in the actively beating ventricle, and this can be achieved only by use of a patch. Actually, more than 50% of the ventricular defects are closed with patches, and my colleagues and I have now operated in 140 cases. In addition, many of the cases of ostium primum, atrioventricular canals, and totally anomalous pulmonary venous drainage require some type of septal substitute.

At present I believe that a knitted crimped Dacron patch serves the purpose better than any material available. This material is obtained from the ends removed from the vascular grafts. It is porous, flexible, and durable and does not fray at the edges. Previous experience with clinical application of autogenous tissue to bridge various portions of the cardiac chambers, as reported by others several years ago, was unsatisfactory. I do not believe the autogenous tissue can compare with synthetic materials for such intracardiac replacements.

DR. HARRIS B. SHUMACKER JR., Indianapolis: I have the feeling that the larger any free autogenous graft is the greater is the likelihood that it will not be vascularized soon enough to permit its survival. Some years ago, after convincing ourselves that the autogenous pericardium was quite suitable for closing experimentally produced atrial septal defects, we applied this procedure in a patient who had a very large defect. When he died five months later, we were amazed to find his defect wide open, with no recognizable remnants of the pericardial graft at all.

DR. HUGH F. FITZPATRICK, New York: I want to thank Dr. Cooley and Dr. Shumacker for their comments. I do not take the position at this time that these grafts will replace Dacron or Ivalon. Our point is simply that at this phase in the study an atrial graft works. It acts as a living framework for connective tissue proliferation, rather than as a prosthetic foreign body, a nonliving framework. It is tissue that is autogenous and possibly (and emotionally) there may be a place for such. As to the size of the graft, we have put them in as large as 6×4 cm. and the same phenomenon occurs. In no instance has there been a disruption or blow-out of the graft. Using atrial grafts, Watkins and Gross found that the autogenous graft was better than the homologous graft.[14]

Observations on Toxicity and Use of Antifoam A

WILLIAM A. REED, M.D., and C. FREDERICK KITTLE, M.D., Kansas City, Kan.

Shortly after beginning an investigation of long-term extracorporeal perfusion in dogs, we were impressed by the number of animals exhibiting postperfusion signs of central nervous system damage. These signs consisted of hemiplegia, skew deviation of the eyes, generalized ataxia, apathy, and apparent blindness. However, these changes were temporary, and by the ninth day after perfusion all such animals had returned to a presumed normal state. Although 16 of 17 consecutive animals perfused for two hours with a plastic disposable bubble-dispersion-type oxygenator * survived, neurologic changes were noted in 50% of the survivors. Gross examination of these animals' brains several weeks later at the time of elective killing disclosed focal areas of infarction. Similar areas of infarction were also noted in animals without clinical signs of central nervous system damage. The possibility of gas, fibrin, or Antifoam A emboli presented itself as a cause of these changes.[14]

Although Antifoam substances have been used in various extracorporeal devices for several years, there is a paucity of data regarding their biologic toxicity and action. Antifoam compounds are polymeric substances with a basic structure of alternating silicon and oxygen atoms. They may take the form of liquids or resins, depending upon their attached radicals. Their use is dependent upon their physical property of a low surface tension. Physiologically they have been presumed inert. Antifoam A, which is a commonly used defoaming substance for many oxygenators, is a rather thick, viscid, water-insoluble methylpolysiloxane compound. Most previous toxicologic studies have been concerned with its cutaneous, oral, or intraperitoneal effects and have been chiefly on rats. These indicated complete lack of or a minimal toxicity. One group of investigators found a nonspecific granulomatous reaction to silicone grease embedded in rats.[9-13,15-20] Surprisingly enough, no detailed studies are available regarding the intravenous or intra-arterial toxicity of this substance, either acute or chronic, or the exact dosage required for effective defoaming.

We have posed three problems regarding the Antifoam A substance as it is used for defoaming in bubble oxygenators.

1. Is the material toxic, and, if so, in what concentration and in what manner?

2. Does the Antifoam A remain in the defoaming chamber, or does it pass into the circulating blood stream?

3. What is the minimum quantity necessary for effective defoaming?

To study the first problem, 31 mongrel dogs, weighing from 8 to 13 kg. and lightly anesthetized with intravenous thiopental (Pentothal) sodium, were used. Varying amounts of Antifoam A were injected into the right external jugular vein during a 10- to 20-second period. The dose was given in one injection and varied from 0.2 to 1.2 ml/kg. (Table 1). The animals considered dead were those dying within 10 minutes after injection, although a few died hours later. The L. D_{50}, as will be noted,

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Markle Scholar in Medical Sciences (Dr. Kittle).

The Department of Surgery, the University of Kansas Medical Center.

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* Travenol Laboratories, Inc., Morton Grove, Ill.

TABLE 1.—*Toxicity of Antifoam A Administered Intravenously (External Jugular Vein) in Thirty-One Dogs*

Dose, Ml/Kg.	Died	Survived
0.2		1
0.3	1	1
0.4		1
0.5		3
0.7		1
0.8	1	2
0.9	2	1
L. D. $_{55}$ 1.0	3	3
1.1	3	1
1.2	6	1
	16	15

(three times weekly) microscopic sections showed focal and diffuse interstitial pulmonary fibrosis (Fig. 1). In other organs evidences of Antifoam A were found microscopically. Routine sections of the kidney revealed globules compatible with the appearance of Antifoam in the glomerular capillaries. Similar globules were noted in the pial vessels.

Since the blood is returned from the extracorporeal device to the arterial circulation, it seemed worth while to determine the intra-arterial toxicity of this substance. A

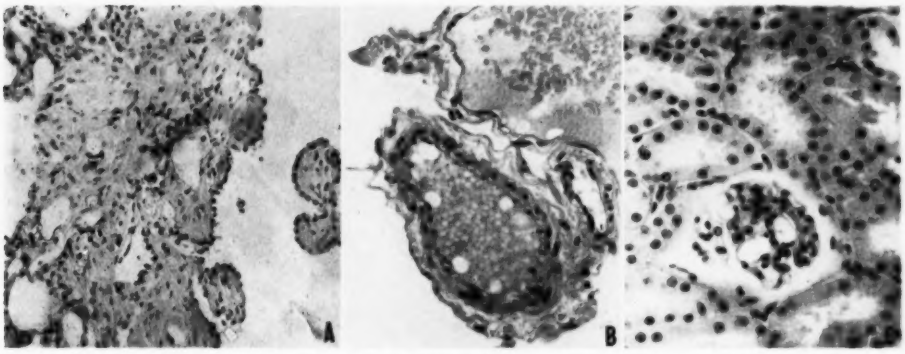

Fig. 1.—*A*, photomicrograph of lung of dog killed three months after receiving 0.4 ml/kg. of Antifoam A intravenously for 11 doses (three times weekly). Focal areas of marked interstitial fibrosis were noted throughout all lobes of the lung.

B, pial vessel containing globules of material resembling Antifoam in dog which had received 0.3 ml/kg. for six injections intravenously (three times weekly).

C, globules in the glomerular capillary with adjacent round-cell infiltration. This dog received 0.3 ml/kg. for six intravenous injections (three times a week).

is approximately 0.9 to 1.0 ml/kg. They pursued a course characteristic for massive pulmonary emboli as evidenced by dyspnea, hypotension, tachycardia, and subsequent death.[1-8] Autopsy in these animals disclosed a grossly distended right ventricle with a comparatively small left ventricle. Small deposits of foreign material resembling Antifoam A could be noted in the subpleural area of these lungs. Those animals which did not die appeared normal.

Chronic toxicity was studied by giving sublethal doses intravenously on repeated occasions. Animals receiving short-term injections (less than three) did not reveal any histologic changes at autopsy. In dogs receiving 11 to 14 injections intravenously

second group, of 27 mongrel dogs, was studied in which varying amounts of Antifoam A were injected into the external maxillary branch of the external carotid artery. This route was chosen for evalua-

TABLE 2.—*Toxicity of Antifoam A Administered Intra-Arterially (External Maxillary Artery in Twenty-Seven Dogs)*

Dose, Ml/Kg.	Died	Survived with CNS Damage	Survived
0.005			1
0.01	1		3
L.D. $_{55}$ 0.02	3	3	3
0.03	5	2	2
0.05	2		
0.10	1		
0.20	1		
0.30	5		

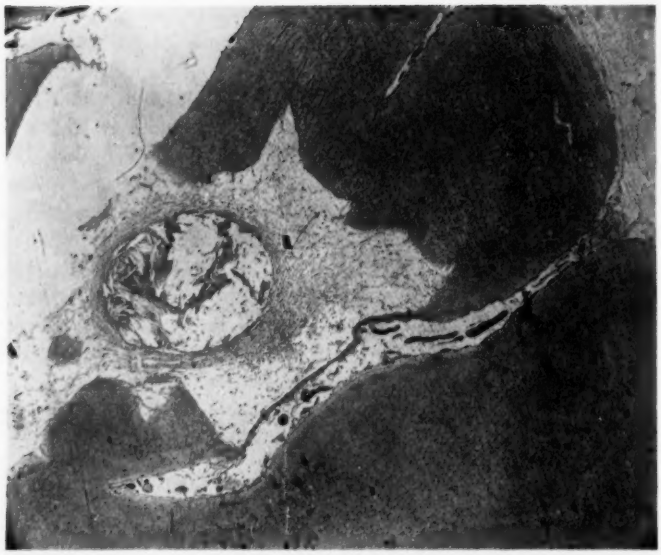

Fig. 2.—Photomicrograph of cerebral cortex with cystic area of degeneration in dog perfused for two hours and killed six months after operation.

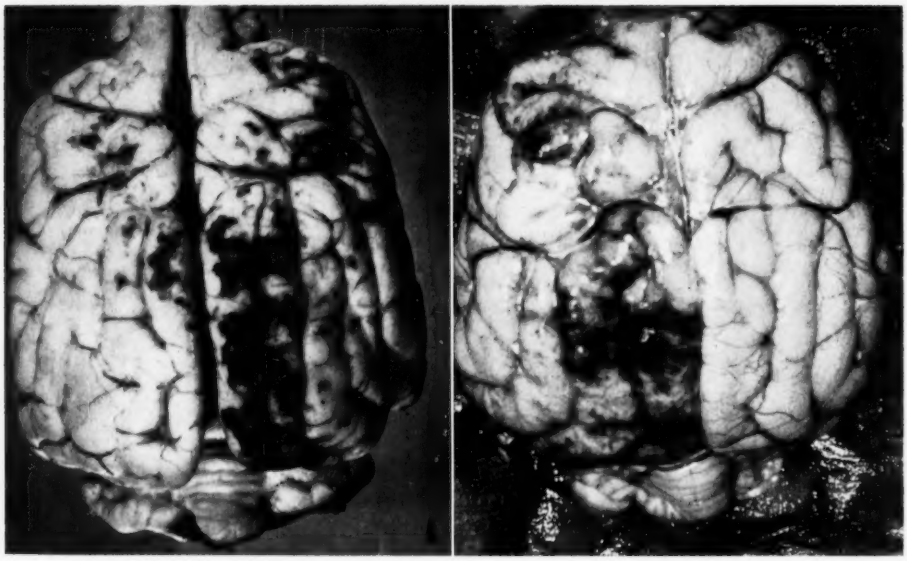

Fig. 3.—*A*, photograph of brain of dog receiving 0.03 ml/kg. of Antifoam in external maxillary artery, showing ipsilateral cerebral infarct with smaller infarcted areas on opposite side. The animal survived injection and had contralateral hemiplegia. It was killed 5 days after injection.

B, brain of dog receiving 0.03 ml/kg. of Antifoam in external maxillary artery, with resultant ipsilateral cerebral infarct. Dog died several hours after injection.

tion of the arterial embolic potential of this substance, although it is recognized that it is not entirely comparable to the clinical situation. It will be noted (Table 2) that much smaller doses caused death, the $L. D._{50}$ being approximately one-fiftieth the intravenous dose. In those animals which died, areas of infarction were noted in the brain. Some animals survived with signs of neurologic damage, chiefly contralateral

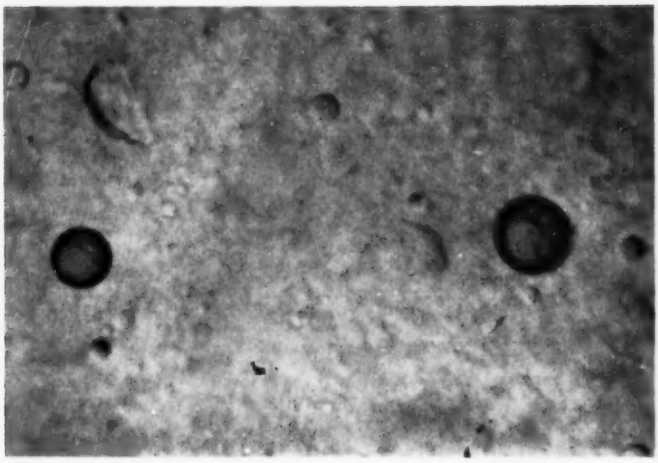

Fig. 4.—Photomicrograph of blood smear taken 30 minutes after perfusion was instituted. Note globules of Antifoam among the blood cells.

hemiplegia. Clinically, these animals resembled those with neurologic changes after prolonged perfusion with the dispersion-type oxygenator (Fig. 2). Subsequent postmortem examination of the paralyzed survivors disclosed focal areas of damage in the brain (Fig. 3).

We have interpreted these observations as indicating that the Antifoam A substance can cause death of the animal or localized tissue damage in an embolic fashion, that intravenously these emboli do not usually pass through the lungs, and that intra-arterially a much smaller dose is lethal or morbid.

Our second problem is concerned with whether or not Antifoam A passes into the circulation during extracorporeal perfusion. To test this, blood smears were made each 15 minutes of blood taken from the arterial side of the oxygenating device during a perfusion experiment. Globules of varying size could be recognized in all such smears from the initial through the two-hour samples (Fig. 4).

It was also noted that during prolonged animal perfusion the initial amount of Antifoam A gradually became ineffective, and additional amounts were required. When the oxygenating apparatus was set up in

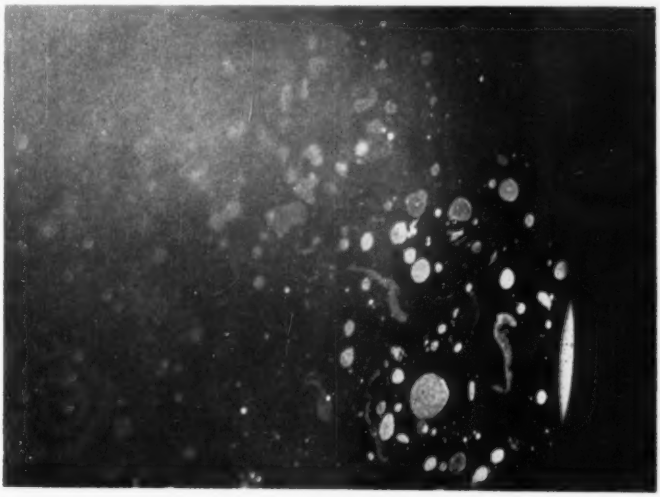

Fig. 5.—Surface of blood drained from oxygenating device after circulation, showing coalesced globules of Antifoam.

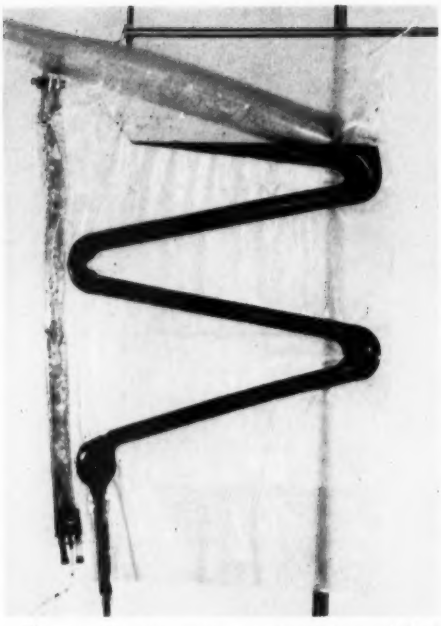

Fig. 6.—Device used to determine minimal amount of Antifoam needed for defoaming. The Antifoam A-ether mixture was autoclaved on the inside of the large plastic tube at the top of the plastic sheet.

the usual manner, but no animal was used, no Antifoam substance was needed after the priming dose. However, when this blood was allowed to settle after it had been recirculated in the above manner, gross globules of Antifoam A appeared on the surface (Fig. 5). This would indicate that initially the Antifoam A is removed from the circulating blood by the animal's tissues.

The minimal amount of Antifoam A to be used is difficult to determine, since conditions of each perfusion present much variation and are dependent upon oxygen flow rate, perfusion rate, temperature of the system, surface upon which the Antifoam is placed, how it has been applied, and other factors.

To answer our third problem, experiments were designed in which the plastic debubbling chamber, as used in the DeWall oxygenator, was adapted to the sheet oxygenator previously described (Fig. 6). Varying amounts of Antifoam A (0.45 to 1.0 ml.) were dissolved in ether to permit even dispersion and were poured in the plastic tube. The ether was then allowed to evaporate. This tube was autoclaved at 252 F for 2 hours 20 minutes.

At a perfusion flow of 1,080 ml/min. and an oxygen flow rate of 3 L./min., defoaming was adequate for 5 minutes with 0.45 ml.; 26 minutes with 0.50 ml.; 42 minutes with 0.55 ml.; over 90 minutes with 0.75 ml., and over 90 minutes with 1.0 ml.

Temperature of the oxygenating apparatus was maintained at 36.0 to 36.5 C throughout the perfusion.

Summary and Conclusions

Antifoam A, a methypolysiloxane, when given intravenously in large doses, may cause death acutely as a pulmonary embolus or chronically cause pulmonary fibrosis.

Intra-arterial injections of Antifoam A cause recognized embolic phenomena in much smaller doses than do intravenous injections.

Antifoam A is transferred from the oxygenator to the blood stream during perfusion.

Antifoam A is effective in defoaming, but judicious care must be exercised regarding the use of this substance.

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DISCUSSION

DR. HARRIS B. SHUMACKER, Indianapolis: This certainly is a nice piece of work, Dr. Reed, regarding an agent which has been used very commonly. If there is no further discussion, would you like to add anything, Sir?

DR. WILLIAM A. REED, I would like to say that we studied only one of many factors which may produce damage during perfusion. We do not propose that Antifoam is the only cause of post-perfusion sequelae.

Surgical Considerations of Peripheral Arterial Aneurysms

Analysis of One Hundred Seven Cases

E. STANLEY CRAWFORD, M.D.; MICHAEL E. DE BAKEY, M.D., and DENTON A. COOLEY, M.D.,
Houston, Texas

Peripheral arterial aneurysms are usually caused by arteriosclerosis, trauma, infection, or poststenotic abnormalities. They occur most frequently in the extremities, since the arteriosclerotic forms are commonest and in the great majority of instances are located in the popliteal or femoral region. Least common is the poststenotic type, which usually occurs in the supraclavicular fossa. Despite differences in etiology and location, these aneurysms are frequently associated with complications that lead to arterial insufficiency, gangrene of the involved extremity, and even death.[11] Treatment usually has been conservative or has consisted of resection without restoration of arterial continuity. Conservative therapy has been associated with subsequent complications in 50% of patients followed from three to five years, and, although excision without arterial reconstruction has provided significant improvement in the treatment of these lesions, many patients continue to have symptoms of arterial insufficiency.[11] Recent developments in arterial replacements for segmental arterial lesions have provided effective methods for restoration of arterial continuity, thus achieving the ideal objective of preserving both function and life of the extremity.[4] The efficacy of this approach is well demonstrated by its successful application in other segmental vascular lesions, as well as by the good results obtained in cases of peripheral aneurysms treated by this method.[1-10,12] The purpose of this report is to present certain observations derived from our experience with 107 cases of peripheral arterial aneurysms in which this therapeutic approach was employed.

Clinical Material

Included in this study are all peripheral aneurysms treated surgically during the past five years other than those occurring within the cranium, thorax, and abdomen, a total of 107 surgically treated cases. Etiologically these aneurysms were classified into five groups, each group to be considered separately (Table 1).

Arteriosclerotic Aneurysms

Among the 54 peripheral arteriosclerotic aneurysms, all but one was located in the popliteal or femoral artery (Table 2). Par-

TABLE 1.—*Etiology of 107 Surgically Treated Peripheral Arterial Aneurysms*

Etiology	No. Cases	Per Cent
Arteriosclerotic	54	50
Traumatic	37	34
Poststenotic	3	3
Aneurysm in homograft	7	7
False aneurysm (postoperative)	6	6
Total	107	100

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Presented at the Sixth Scientific Meeting of the North American Chapter of the International Cardiovascular Society, San Francisco, June 21, 1958.

From the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, and the surgical services of the Jefferson Davis, Veterans Administration, and Methodist Hospitals.

TABLE 2.—*Location of Fifty-Four Surgically Treated Peripheral Arteriosclerotic Aneurysms*

Location	No. Cases	Per Cent
Popliteal artery	30	55
Femoral artery	23	42
Innominate artery bifurcation	1	2
Total	54	99

ticularly significant is the high incidence of multiple lesions in this group of patients (Table 3), as compared with the relatively low incidence of this occurrence in patients with aneurysms of the aorta. Whereas 55% of the former group of patients had more than one aneurysm, in our series of 650 cases of aneurysms of the aorta, the incidence of multiple lesions has been less than 5%.

TABLE 3.—*Incidence of Multiple Aneurysms Associated with Peripheral Arteriosclerotic Aneurysms*

Location of Lesion	No. Patients	Per Cent
Bilateral popliteal aneurysm	5	10
Bilateral femoral aneurysm	3	6
Femoral and popliteal aneurysm	3	6
Associated aortic and iliac	15	32
Total	26	54

All of the patients except one in this series were men, the oldest being 85 and the youngest 45 years of age, with 95% in the sixth and seventh decades of life. As previously indicated,[6,8,9] in patients with other arteriosclerotic lesions the incidence of associated cardiovascular disease was relatively high (Table 4). The presence of these associated lesions was not considered significant in selection of patients for operation, although patients with severe angina pectoris, intractable cardiac failure, and moderately advanced renal insufficiency were excluded from operative treatment unless the alternative was likely to be amputation.

TABLE 4.—*Incidence of Cardiovascular Disease Associated with Fifty-Four Cases of Peripheral Arteriosclerotic Aneurysms*

Disease	No. Patients	Per Cent
Heart disease	24	51
Hypertension	21	40
Cerebrovascular accident	4	10
Other aneurysms	26	55

TABLE 5.—*Symptoms Associated with Peripheral Arteriosclerotic Aneurysms*

Symptoms		No. Patients	Per Cent
Mass		32	70
Pulsatile	10		
Painful	13		
Enlarging	4		
Local pain (mass unknown)		4	8
Intermittent claudication		24	50
Rest pain		7	15

The clinical manifestations of femoral and popliteal aneurysms were essentially the same in these cases (Tables 5 and 6). The aneurysms had produced significant disturbances in the great majority of patients, and these changes had reached a sufficient degree of severity to threaten life or limb in approximately half the cases. Of particular significance in this connection is the fact that four patients in this series had had amputation of the opposite extremity for complications resulting from an aneurysm.

Treatment was directed toward excision of the lesion and restoration of normal blood flow, except in the presence of irreversible gangrene involving a major part of the extremity (Table 7). Successful treatment was dependent upon certain favorable pathologic features of the disease, including localization of the lesion to a segment of artery of sufficient size to per-

TABLE 6.—*Complications Associated with Peripheral Arteriosclerotic Aneurysms Occurring Before Admission to Hospital*

Complications	No. Cases	Per Cent
Thrombosis	16	34
Rupture	8	17
Arterial insufficiency	24	51
Previous leg amputation (opposite side for aneurysm)	4	9
Associated rupture of abdominal aneurysm	2	4

TABLE 7.—*Operations Employed in Fifty-Four Peripheral Arteriosclerotic Aneurysms*

Operation	No. Cases	Per Cent	Successful Results * No. Cases	Successful Results * Per Cent
Excision and graft replacement	32	60	28	90
Excision and end-to-end anast.	14	26	13	93
Graft bypass	7	13	6	85
Primary amputation	1	2	0	0
Total	54	100	47	87

* Failures include amputation in four patients and death in three patients.

mit direct attack and reasonably normal patent arterial channels both above and below the lesion. The latter requirement assumed great importance, considering the frequency of complications leading to arterial occlusion prior to treatment (Table 6). The arteriographic and pathologic studies and the operative findings in this series of patients indicate that favorable circumstances for reconstructive operation were present in most cases. The arterial channels proximal to the lesion were patent at some level in all cases; consequently, the critical factor in the application of a reconstructive operation was patency of the distal segment. The condition of the distal segment varied in patients with thrombosed or nonpulsating aneurysms, and patency was dependent upon the degree of collateral blood flow. A patent segment adequate for reconstructive operation was invariably present in those patients with good peripheral circulation at rest, whereas in patients with severe arterial insufficiency the distal segment was usually occluded. Most of the latter patients had had recent thrombosis of the aneurysm with distal propagation of the thrombus. In some of these patients without irreversible gangrenous changes, it was possible to remove the thrombus from the distal segment and restore normal distal circulation.

Consequent to finding these fortunate pathologic characteristics, all patients were considered candidates for operation, and the type of procedure was determined by the nature and extent of the lesion: For example, 14 small aneurysms (4 femoral and 10 popliteal), involving only a short segment of artery, were satisfactorily excised and arterial continuity restored by simple end-to-end suture of the uninvolved proximal and distal segments. In some instances, mobilization of the artery above and below the aneurysm and flexion of the knee, as originally recommended by Enderlen,[10] were required to bring the segments together without excessive tension. Knee flexion, when required, was maintained by

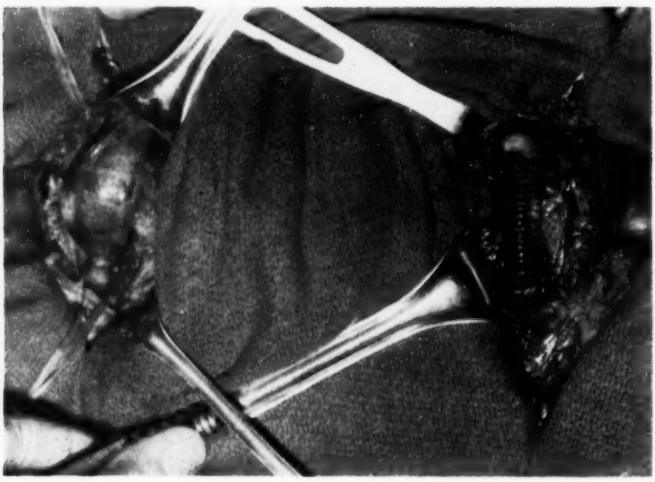

Fig. 1—Photograph taken at operation in patient with bilateral femoral artery aneurysms. The aneurysm on the left has been replaced with a segment of the new Dacron tube, and the aneurysm on the right has been isolated in preparation for the same procedure.

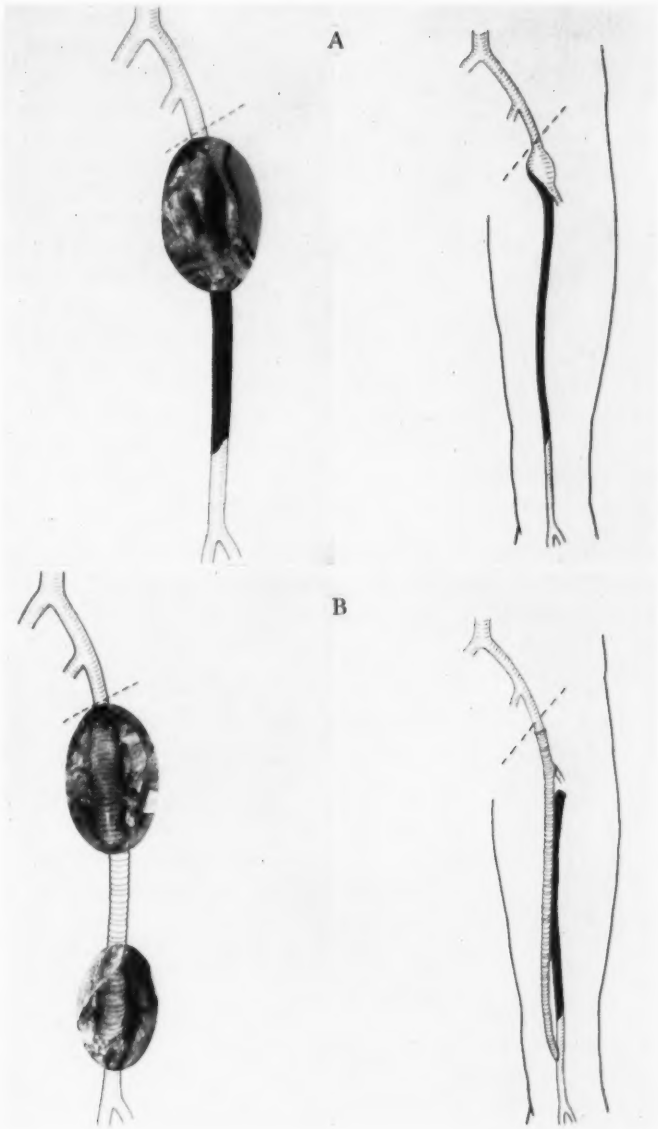

Fig. 2.—*A*, Photograph taken at operation and diagrams showing aneurysm of the common femoral artery associated with segmental occlusion of the superficial femoral artery and patency of the deep femoral artery. *B*, photograph taken at operation and diagrams showing Dacron tube replacing the aneurysm and bypassing the segmental occlusion of superficial femoral artery. Restoration of circulation to the thigh is evident by anastomosis between the graft and the deep femoral artery.

posterior plaster splint for one week. In the seven, 32 aneurysms (17 femoral and 15 popliteal) were relatively large and involved a long segment of artery. After excision of the aneurysm in these cases a suitable arterial replacement was required to bridge the defect and restore arterial continuity (Fig. 1). In seven cases the lesion was associated with multiple aneurysms, arteriosclerotic occlusive vascular disease, or extensive thrombosis. In such cases it was simpler to restore circulation either by excising the aneurysm and inserting a bypass graft or, when thrombosis had occurred, by bypassing completely the occluded segment, leaving it undisturbed by attaching the ends of the graft to the common femoral artery, above, and the distal

TABLE 8.—*Arterial Replacement Employed in Thirty-Nine Peripheral Arteriosclerotic Aneurysms*

Type of Replacement	No. Cases	Per Cent	Successful Results: No.	Successful Results: Per Cent
Homograft	15	40	14	93
Dacron	20	51	17	85
Edwards-Tapp	4	10	3	75
Total	39	100	34	87

portion of the popliteal artery, below, (Fig. 2). Thus, an operation performed through two small incisions connected by a tunnel made by blunt dissection greatly simplified the approach in this type of problem.[2] Of the six patients with peripheral gangrene, only one was subjected to primary amputation without previous attempts at reconstructive operation. The successful application of graft operations in 39 cases required the availability of a satisfactory arterial substitute (Table 8). Although a high degree of success was obtained with the use of various types of vascular replacements, a new Dacron tube has in our experience been the most satisfactory, for several reasons.[4-6] First, the problems of procurement, preparation, and storage associated with homografts have been obviated. Second, because of its physical properties and method of construction, the Dacron tube is technically more suitable than either the Edwards-Tapp nylon tube or the arterial homograft. Finally, follow-up studies appear to confirm the superiority of this material by the fact that fewer complications and late failures have occurred following use of this tube.

TABLE 9.—*Results in Patients Surviving Operation for Arteriosclerotic Femoral and Popliteal Aneurysms*

Status of Pedal Pulses Before Operation	No. Cases	Per Cent	Pulse Restored: No.	Pulse Restored: Per Cent	Amputation: No.	Amputation: Per Cent
Pulses absent	21	42	15	71	4*	19
Pulses present	29	58	28	96	0	0
Total	50	100	43	86	4*	8

*Amputation was required in four of the six cases with gangrenous changes secondary to acute thrombosis of the aneurysm.

Despite the factors of operative risk and advanced stages of ischemic damage in some patients, the results in these cases were highly gratifying and did not vary significantly with the type of operation employed (Tables 7-9). Amputation was required in only 4 patients, although gangrenous changes were present in 6 and signs of less severe arterial insufficiency in 24 patients prior to operation. In the remaining cases, peripheral pulses were restored and the patient was relieved of symptoms except in three patients, who continued to complain of mild intermittent claudication. Death occurred in the immediate postoperative period in only three patients, despite the high incidence of associated cardiovascular diseases and the removal of associated abdominal aortic aneurysms in a significant number of patients. Death occurred from myocardial infarction in two patients, one with a ruptured abdominal aortic aneurysm and a thrombosed femoral aneurysm associated with acute severe arterial insufficiency of the leg, and the other, an 84-year-old man with a ruptured popliteal aneurysm. Death in the third patient was due to massive air embolism resulting from a transfusion accident during operation.

These patients have been followed regularly since operation, in some instances up to five years, and the results continue to be

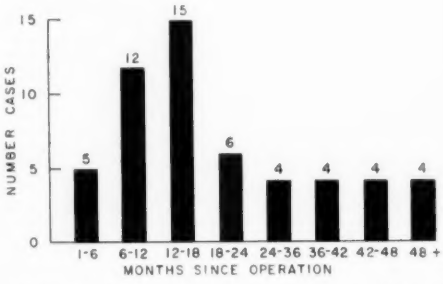

Fig. 3.—Distribution of cases with peripheral arteriosclerotic aneurysm treated during the past five years.

most gratifying (Fig. 3). Death has occurred after operation in only three patients —one two years later, from a ruptured abdominal aortic aneurysm; one eight months later, from cancer, and one six months later, from myocardial infarction. Although arterial occlusion occurred in two patients six and eight months, respectively, after excision of popliteal aneurysms and primary end-to-end anastomosis of the uninvolved arterial segments, amputation has not been required in any case after discharge from the hospital. The replacement has remained patent, and good peripheral circulation persists in all patients in whom this procedure was successfully employed in the treatment of peripheral aneurysm.

The fact that only one peripheral arteriosclerotic aneurysm in this series of 54 cases did not involve either the femoral or the popliteal artery indicates the rarity of such lesions. The aneurysm in this case, previously reported in detail,[7] was located at the bifurcation of the innominate artery and involved the innominate, subclavian, and right common carotid arteries. This patient complained of an enlarging, painful, pulsating mass at the base of the right side of the neck, and physical examination revealed at 2.5×3 cm. mass in this region, with palpable distal pulses. Successful excision and homograft replacement were performed, employing a temporary shunt to maintain circulation during operation. It has been almost three years since operation, and the result in this case continues to be very satisfactory.

Traumatic Aneurysms

As might be expected, traumatic aneurysms are more likely to occur in younger persons than arteriosclerotic aneurysms. This is well exemplified in this series of 37 patients whose ages range from 10 to 56 years with the highest incidence occurring in the third and fourth decades of life. The injury consisted of a gunshot wound in 25 patients and a stab wound in 12 patients. The lesion was a false aneurysm in 12 patients, and in 25 patients the predominant lesion was an arteriovenous fistula, which in most instances was associated with a false aneurysm. Although the duration of the lesion ranged from 2 hours to 27 years, in most cases this was measurable in terms of weeks, and, as a result of more aggressive treatment of acute arterial injuries, the recent cases were all treated within a few hours of injury. While there was wide variation in the site of injury, the lesion was located in an artery essential for normal blood flow to the part in 29 cases (80%). The carotid artery was involved in 4 patients (11%), the brachial artery in 12 (32%), the femoral artery in 6 (16%), the popliteal artery in 6 (16%), and the subclavian artery in 1 (2%). In the remaining eight patients (20%) the lesion involved minor arterial branches.

The clinical manifestations of the lesion were usually similar. Most patients complained of a pulsating mass existing from the time of injury, and those with arteriovenous fistulae were aware of a buzzing sensation in the region of the mass. In 6 patients there was associated nerve injury, 5 cases occurring in the 12 patients with brachial-artery lesions, and in one case partial facial paralysis was associated with an external maxillary arterial and venous fistula. Cardiac failure was present in 3 of the 25 patients with arteriovenous fistula. The fistulae in these cases were located in the carotid, brachial, and popliteal arteries and had been present for 27, 12, and 3 years in patients who were, respectively, 54, 38, and 33 years of age. In the remaining patients with arteriovenous fistula, the lesions had been present less than 26 months, and usually for only a few weeks; but, despite the lack of cardiac failure, some of these patients had cardiac enlargement, as seen by roentgenographic examination. The presence of a continuous thrill or bruit on physical examination differentiated accurately an arteriovenous fistula from a simple false aneurysm, which presented only

Fig. 4.—Illustrations of false aneurysm of the right brachial artery showing (*A*) the specimen and its arteriographic appearance, (*B*) the lesion at operation, and (*C*) restoration of normal circulation by excision and end-to-end anastomosis of the uninvolved arterial segments.

a pulsating mass and a systolic murmur. Pulses were absent distal to the lesion in two cases. One of these patients had had a false aneurysm of the popliteal artery for 12 years, and the other had had an arteriovenous fistula between the popliteal artery and vein for 25 years. These patients complained of intermittent claudication, in addition to the symptoms previously described.

Treatment in these cases consisted of excision of the lesion and restoration of normal arterial blood flow when necessary to maintain normal circulation in the involved part. In the 29 patients in whom the aneurysm involved a major artery, such as the carotid, arterial continuity was restored by primary end-to-end anastomosis of the uninvolved proximal and distal segments (Fig. 4). In eight patients ligation of the proximal and distal segments was performed after excision of lesions involving arteries that did not contribute significantly to the circulation of the involved part. The arteries ligated in these cases were the ulnar, radial, posterior tibial, pedal, external

maxillary, peroneal, and temporal. The safety of ligation in these cases involving an extremity was determined at operation by persistence of pulses in the hand or foot. Maintenance of circulation by temporary shunts or cerebral protection employing hypothermia was not considered necessary during the period of arterial occlusion in the treatment of patients with traumatic lesions of the carotid artery. A previous study of 18 traumatic lesions of the carotid artery indicated that these procedures were unnecessary, provided that the operation was expeditiously conducted and normal circulation restored.[3]

The results in these cases were excellent. All patients survived operation, and normal circulation was restored in 28 of the 29 patients in whom the lesions were treated by excision and restoration of arterial continuity. Failure to restore normal circulation occurred in one of the two patients who had intermittent claudication and occlusion of the popliteal artery beyond the lesion. The distal occlusion in this patient was diffuse and extended well down into the small arteries of the calf, making direct anastomosis impossible. Although a distal pulsatile blood flow was not restored in this case, the condition of the circulation remained unchanged, and the patient was cured of his cardiac abnormalities. Symptomatic relief was obtained in all the remaining cases, and continuous follow-up examinations, extending up to five years after operation, indicate persistence of these good results.

Poststenotic Aneurysms

The most frequent cause of poststenotic aneurysm is coarctation of the aorta, but occasionally such lesions occur in the major peripheral arteries and are most frequently located in the subclavian artery just distal to a constriction produced by the scalenus anticus and the first rib or a cervical rib.

Only three lesions of this type occurred in our series (Fig. 5*B*). The ages of these patients were 25, 35, and 57 years, respectively, and the duration of the abnormality was five years in two patients and six years in the other. An enlarging, painful mass had been complained of by all these patients, and, although all had been pulsatile, one had ceased pulsating prior to hospital admission and was associated with pain, which radiated down the arm. The aneurysm in these patients was located in the supraclavicular fossa, two on the right side and one on the left side (Fig. 5*A*). Peripheral pulses were normal in the two patients with pulsatile aneurysms and absent in the patient with the thrombosed lesion.

The factors considered essential for definitive therapy in these cases were release of arterial constriction, excision of the lesion, and restoration of arterial continuity. Arterial constriction was relieved by dividing the anterior scalene muscle, employing the necessary precautions to prevent injury to the phrenic nerve; and excision was performed after control had been obtained by temporary arterial occlusion both proximal and distal to the lesion (Fig. 5*C*). Arterial continuity was restored by end-to-end suture of the uninvolved arterial segments in two cases (Fig. 5*E*). The lesion in the third patient consisted of a thrombosed aneurysm and an occluded segment of artery both proximal and distal to the aneurysm. The sizable defect remaining in this case after excision of the entire abnormal arterial segment required the use of an arterial replacement for arterial reconstruction, and the case being an earlier one, an arterial homograft was employed for this purpose. Operation was performed in all cases through an oblique supraclavicular incision without cutting the clavicle. Normal peripheral circulation was restored in these patients, and recent follow-up examination indicates persistence of these results in two patients. Death due to muscular dystrophy occurred in the other patient two years after operation.

Aneurysms Arising in Homografts

During the past five and one-half years we have resected more than 98 peripheral segmental vascular lesions with homograft

Fig. 5.—Photographs of aneurysm in the right subclavian artery, presenting clinically as (*A*) a mass in the supraclavicular fossa, located (*B*) immediately distal to the anterior scalenus muscle, treated (*C*) by dividing the scalenus muscle, removing the aneurysm (*D*), and restoring circulation (*E*) by end-to-end suture of the uninvolved segments of the artery.

replacement. Although the last homograft was employed over 18 months ago, only seven aneurysms have been known to develop in these cases. This complication developed in the femoral segment of a homograft employed in one case to bypass an occlusion of the iliac artery, and examination of the removed specimen indicated that the aneurysm had developed in the region of injury occurring during operation. The aneurysm in this case became evident eight months after operation, with the onset of acute arterial insufficiency resulting from thrombosis of the aneurysm. Normal circulation was successfully restored in this patient by removal of the involved homograft and thromboendarterectomy of the occluded iliac artery. Aneurysms developed in three different homografts in each of two other patients. In one of these patients an aneurysm developed 18 months after operation in each

of the three segments of iliac artery homografts joined together by end-to-end suture and employed as a femoral end-to-side bypass graft. Aneurysms developed in homografts employed in the other patient to bypass occlusions of the right iliac and left superficial femoral arteries. The complication became evident in the femoral segment of the iliac graft 16 months after operation. The involved homograft was successfully removed and replaced by a new homograft; however, 10 months later an aneurysm developed in both this graft and the homograft previously inserted to bypass the left femoral occlusion. The lesions in both these patients were successfully treated by removing the homografts and replacing them with nylon tubes, and to date, 16 months after the last operation, aneurysms have not recurred in the region of the tubes, which continue to function and provide normal peripheral circulation.

The basis for the development of this complication in the homografts used in the latter two patients is not clear. Each segment of graft employed in these cases was obtained from a different donor, and collected, prepared, and stored separately by the freeze-drying method. In one patient the grafts were inserted in separate incisions on different occasions. Consequent to these variables, an abnormal immunologic response may be considered a factor in the development of this complication in these cases; however, such a response could never be established in either case.

False Aneurysms Occurring at the Suture Line

False aneurysms developed at one of the suture lines in six patients in whom synthetic arterial substitutes were employed to bypass peripheral occlusive lesions occurring in the external iliac artery of one patient and the superficial femoral artery of five patients. The Edwards-Tapp nylon tube had been employed as the bypass in five patients, and in the other patient a knitted Dacron tube had been used. The aneurysm was located at the junction of the common femoral artery and the Edwards-Tapp tube in four cases and at the junction of the Edwards-Tapp tube and the popliteal artery in one case. The false aneurysm in the patient in whom the Dacron tube was employed occurred at the junction of the tube and the popliteal artery. The complications in these patients occurred 16 days to 3 months after operation and became evident by the appearance of a rapidly enlarging, painful, pulsatile mass and mild elevation of temperature. Good peripheral pulsatile circulation was present distal to the lesion in all cases.

The etiologic factors in the production of these lesions were infection, excessive tension at the suture line, traction on the anastomosis produced by motions of the associated joints, and certain structural defects of the graft materials. Pyogenic organisms (Staphylococcus aureus) were cultured from the wounds in all cases. The occurrence of this complication suggests that the material or its structural characteristics were of some significance, particularly the nylon tube, which was associated with all but one of these complications. Fraying at the ends of the graft when inserted under tension occurred only with the use of the Edwards-Tapp nylon tube. It was evident at reoperation that this destructive mechanism increased after operation and was due to excessive tension at the time of insertion, which was increased after operation by motion in the hip and knee joints. The significance of motion after operation is evident by the fact that in all cases except one the complications occurred in an anastomosis located in the region of a joint. The arterial wound separation occurred in the patient in whom the Dacron tube was employed was caused by infection and excessive tension resulting from extension of the knee and the insertion of a tube of insufficient length to permit the required range of motion.

Treatment in these cases was directed toward the production of hemostasis, steri-

lization of the wound, and restoration of arterial continuity. Wound sterilization in these cases was achieved by evacuation of all blood clots, debridement of devitalized tissue, copious irrigation with neomycin and bacitracin solution, and careful, complete closure of the wound. The appropriate antibiotics were given after operation in large doses. In an attempt to produce hemostasis and restore normal arterial continuity, a number of procedures were employed. The opening at the anastomosis was closed by a simple over-and-over suture in three patients, and a new tube was inserted as a bypass graft in the other three cases. A normal pulsatile circulation was temporarily restored in all of these patients; however, recurrence of the complication developed in four patients within three months requiring removal of the tubes and arterial ligation. In the other two patients, the wounds healed, and the grafts continue to function up to the present time, over one year after operation. Amputation was required in only two of the patients in whom graft removal and artery ligation were necessary.

Summary

Peripheral aneurysms may result from a variety of conditions, such as arteriosclerosis, trauma, infection, and poststenotic abnormalities, but, despite these differences in etiology, they are frequently associated in their natural course with complications which lead to arterial insufficiency, gangrene, and even death of the patient. Treatment has usually been conservative or resection without restoration of circulation. The high incidence of complications associated with conservative therapy and the production of arterial insufficiency by excision without arterial reconstruction have emphasized the limitations of these forms of treatment. The recent advances in arterial reconstructive surgery have provided the opportunity and stimulus both to excise the lesion and to restore arterial continuity, thus achieving the ideal objective in the therapy of these lesions.

This report is concerned with the application of this approach in the treatment of 107 cases of peripheral arterial aneurysms during the past five years. In this series of surgically treated cases, there were 54 arteriosclerotic aneurysms, 37 of traumatic origin, 7 occurring in homografts, 6 false aneurysms occurring after peripheral arterial operations, and 3 poststenotic aneurysms of the subclavian artery. Of the 54 arteriosclerotic aneurysms, 30 were located in the popliteal artery, 23 in the femoral artery, and 1 at the bifurcation of the innominate artery. The relatively high incidence of multiple lesions in this group of peripheral arteriosclerotic aneurysms is evident from the fact that more than one aneurysm was present in 55% of the cases. Traumatic aneurysm was present in 37 patients and resulted from a gunshot wound in 25 and a stab wound in 12 cases. The lesion was a false aneurysm in 12 cases, and in 25 cases there were both a false aneurysm and an arteriovenous fistula. These traumatic lesions were widely distributed, but in 29 patients (80%) the aneurysm involved an artery necessary for normal blood flow, such as the carotid, brachial, femoral, popliteal, or subclavian.

Poststenotic aneurysms occurred in three patients and were located in the subclavian artery just distal to a constriction produced by the anterior scalenus muscle. Aneurysms developed in seven peripheral homografts employed in the treatment of occlusive lesions of the femoral artery in three patients 8 to 26 minutes after operation. Trauma was the cause of the aneurysm in one of these cases, and an abnormal immunologic response was suggested but not proved in the remaining cases. The etiologic factor in the development of the false aneurysms occurring after operation was a combination of infection, tension at the suture line, and fraying associated with the use of the Edwards-Tapp nylon tube.

The clinical manifestations of the disease varied according to the type of lesion. For example, patients with arteriosclerotic aneu-

rysms were considerably older than the other patients and frequently had associated heart disease and hypertension. The presenting symptom in the majority of patients, regardless of the type of lesion, was a pulsating mass. Thrombosis was present in a significant number of cases, and this complication was associated with arterial insufficiency in all cases. Rupture had occurred in eight patients with arteriosclerotic aneurysms, and heart failure was present in three patients with arteriovenous fistulae.

The lesion was localized to an operable segment of artery in all cases, and treatment was directed at both excision of the lesion and restoration of circulation. The aneurysms were excised in all patients, and restoration of circulation was possible by end-to-end suture of the uninvolved segments in 45 cases—14 arteriosclerotic, 29 traumatic, and 2 poststenotic aneurysms of the subclavian artery. The defect remaining after excision of the lesion in the other patients was of sufficient length to require an arterial substitute to restore peripheral circulation. Homografts, Dacron tubes, and the Edwards-Tapp tube were used for this purpose.

The results obtained in these cases were extremely gratifying, particularly when compared with the natural course of the disease. Normal circulation was restored in the majority of these patients. Amputation was required in only six patients, although a larger number had arterial insufficiency and gangrene at the time of operation. Death occurred in only three patients in this series, all of whom had arteriosclerotic aneurysms, despite the high incidence of associated heart disease and hypertension. Death occurred from myocardial infarction in two patients operated upon for rupture of the aneurysm. Death in the other patient was from air embolism. Although the follow-up period has been over three and one-half years in most instances, the results have been well maintained. Three patients with arteriosclerotic aneurysms have died since operation, one from a ruptured aortic aneurysm, one from myocardial infarction, and one from cancer. Arterial occlusion has occurred in only three cases, and amputation has not been required in any case since discharge from the hospital.

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DISCUSSION

Dr. Norman E. Freeman, San Francisco: This is a beautiful paper, and I am delighted to hear Dr. De Bakey call attention to the involvement of various portions of the arterial system in cases of aneurysm. Dr. Williams, the radiologist at the Franklin Hospital (San Francisco), has termed this condition "aneurysmosis." We always look for, and not infrequently find, more than one aneurysm in patients who develop a popliteal aneurysm. Our treatment during the last few years has been the use of the crimped nylon graft. I think this graft is especially useful in the popliteal artery in patients with arteriosclerotic aneurysms, because the arterial wall is dilated and it is possible to use a graft with a large internal diameter. (Slide) This is a picture of a patient who had a thrombosed popliteal aneurysm and upon whom a simple bypass operation was performed, leaving the aneurysm in situ. I know it is supposed to be dangerous to leave an aneurysm in situ, but this patient had recovered for several months and the vessels were well healed. He apparently had adequate circulation above and below—a good popliteal artery below and good segment above. This crimped nylon graft, as you see, does very well in the flexion of the knee. We have used this crimped nylon in a series of nine cases and have been very well satisfied with its use. Again, I want to say how much I enjoyed these papers.

Dr. David I. Abramson, Chicago: I believe that Dr. De Bakey stated that he thought the intermittent claudication was related to the aneurysm. I don't quite understand the hemodynamics associated with such a situation, and I'd like to ask him to explain this. If there were no impingement upon the lumen, I would assume that there would be no interference with blood flow and, consequently, no signs of intermittent claudication. A better explanation might be that the intermittent claudication was due to the same underlying condition responsible for the aneurysm, namely, arteriosclerotic changes in the aorta at the level of the aneurysm.

Dr. Michael E. De Bakey, Houston, Texas: We have employed various types of synthetic grafts for several years. During the past year and a half, however, we have used almost exclusively our knitted Dacron graft because it has proved so satisfactory.

As regards the question of treating these peripheral aneurysms by means of the bypass procedure without removal of the aneurysm, an important consideration is the fact that so long as blood flow through the aneurysm is permitted there exists the threat of complications, such as rupture. Even if thrombosis in the aneurysm occurs, there is the possibility of necrosis and infection. For these reasons we believe resection of the aneurysm is preferable.

In response to Dr. Abramson's question concerning the occurrence of intermittent claudication, I believe that in most instances this is due to occlusion from thrombosis in the aneurysm. This is further supported by the fact that in the majority of our cases in which this occurred and in which the distal arterial segment was patent, circulation was restored and intermittent claudication was relieved.

Fate of Aortic Homografts in Experimental Canine Atherosclerosis

II. Study of Fresh Abdominal Aortic Implants into Abdominal Aorta

HENRY HAIMOVICI, M.D.; NELICIA MAIER, M.D., Ph.D., and LOTTE STRAUSS, M.D., New York

In a previous investigation [1] it was shown that fresh homologous thoracic aortic implants into the abdominal aorta of dogs receiving a chronic atherogenic diet exhibited minimal or no atheromatous changes, while extensive lesions were found in the host abdominal aorta. It appeared from this study that fresh thoracic homografts showed far less susceptibility to atherosclerosis than the host abdominal aorta. These findings, coupled with our previous study showing a metabolic difference between thoracic and abdominal aorta in the dog,[2,3] suggested the existence of a biologic dissimilarity between the two aortic segments.

To test this hypothesis further, another series of experiments was undertaken in which fresh abdominal aortic homografts were implanted into the abdominal aorta.

The present study is concerned with the fate of these grafts investigated by histological and biochemical methods.

Material and Methods

Fourteen mongrel dogs, ranging in age from 1 to 3 years and weighing between 11.0 and 20.0 kg., were used. Sterile homologous segments of the infrarenal abdominal aorta freshly secured were implanted into the abdominal aorta of dogs, below the renal and above the inferior mesenteric arteries. The diameter of the implants was carefully matched with that of the host abdominal aorta. A few weeks after implantation of the graft eight dogs were placed on a cholesterol-thiouracil regimen, and six were given 1 mc. of radioactive iodine per kilogram and placed on a cholesterol diet. In two of the six dogs having received radioactive iodine, the level of serum cholesterol appeared inadequate, and thiouracil in a dose of 60-70 mg. per kilogram was added to the diet daily. The diet and the amounts of cholesterol and thiouracil were as described in the previous paper.[1] Blood cholesterol levels were determined biweekly by the method of Abell et al.[4] The dogs were killed 3½ to 12 months after onset of the atherogenic regimen. At autopsy, the entire cardiovascular system was examined and careful notations made of all lesions present. Microscopic studies of the graft and adjacent host aorta were done routinely. Hematoxylin-eosin and Weigert elastica-Van Gieson stains were used for all sections. Study of succinic dehydrogenase and cytochrome oxidase systems in the graft and adjacent host aorta was also done, using the Warburg technique.[5]

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From the Henry and Lucy Moses Research Laboratory of the Surgical Division, Montefiore Hospital, and the Pathology Department, Mount Sinai Hospital.

Results

The average serum cholesterol values ranged from 721 to 2,340 mg. per 100 cc. (Table 1). Statistical distribution of hypercholesteremia was slightly below 1,000 mg. in 21.4%, above 1,000 mg. in 71.4%, and above 2,000 mg. in 7.2% of the dogs. Both a sustained high level of hypercholesteremia and its duration of five to six months appeared to account for the pronounced degree and extent of the atherosclerotic lesions, although in some instances, as already previously reported,[1] such correlation did not seem to exist.

Atheromatous lesions were present in variable degrees throughout the arterial system in all dogs. The arch and descending thoracic aorta were free of atherosclerosis

TABLE 1.—*Serum Cholesterol Levels and Degree of Atherosclerosis in Dogs on a Chronic Cholesterol-Thiouracil or Cholesterol-Radioactive Iodine Regimen*

Dog	No.	Date of Implant	Duration Graft Implanted, Mo.	Duration Atherogenic Regimen, Mo.	Average Serum Cholesterol, Mg/100 Cc.	Degree of Atherosclerosis
1	912	3/8/57	11 ¾	9 ¾	721 (372-1,378)	++
2 *	917	3/29/57	12 ¾	11 ½	1,510 (794-2,562)	+++
3 *	918	3/22/57	12	10	1,256 (656-1,860)	+++
4 *	921	4/12/57	13	12 ½	992 (473-2,518)	++
5	923	8/21/57	8 ¼	6 ½	1,480 (732-2,260)	++++
6	925	5/17/57	4 ¼	4	1,808 (1,025-2,655)	++++
7 *	926	4/26/57	12 ½	11	928 (552-1,360)	+++
8 *	927 †	6/7/57	4	3 ¼	1,246 (1,060-1,542)	—
9	933	6/21/57	8 ¼	7 ¼	2,340 (1,582-2,984)	++++
10	934	6/14/57	8	6 ¾	1,039 (485-1,570)	+++
11 *	936	6/21/57	9 ¼	8 ¾	1,441 (430-2,542)	++++
12	937	10/17/57	6	5 ¾	1,011 (716-1,328)	++
13	938 †	1/15/57	7	5 ¼	1,305 (632-2,286)	++
14	939	1/29/58	6 ¾	5 ½	1,786 (652-2,500)	+++

* Dogs on cholesterol-radioactive iodine regimen.
† Graft thrombosed.

in all, except in two cases, in which superficial atheromatous streaks were present along the ostia of the intercostal arteries, and in one case, in which a more extensive but superficial atheromatous deposit was noted. The abdominal aorta and the medium-sized and small arteries were involved in almost all instances. In the last two groups of arteries the lesions ranged in degree of severity from early atheromatous plaques to complete occlusion of the lumen, with all the intermediate stages of the atherosclerotic process. A detailed study of these lesions will be reported elsewhere.

The host abdominal aorta, both proximal and distal to the graft, was involved in 12 of 14 cases, the degree of involvement of the atheromatous lesions ranging from

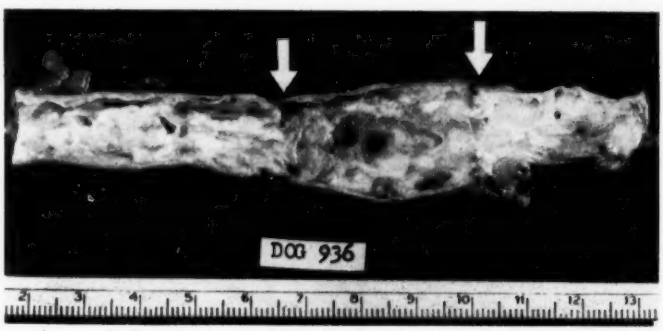
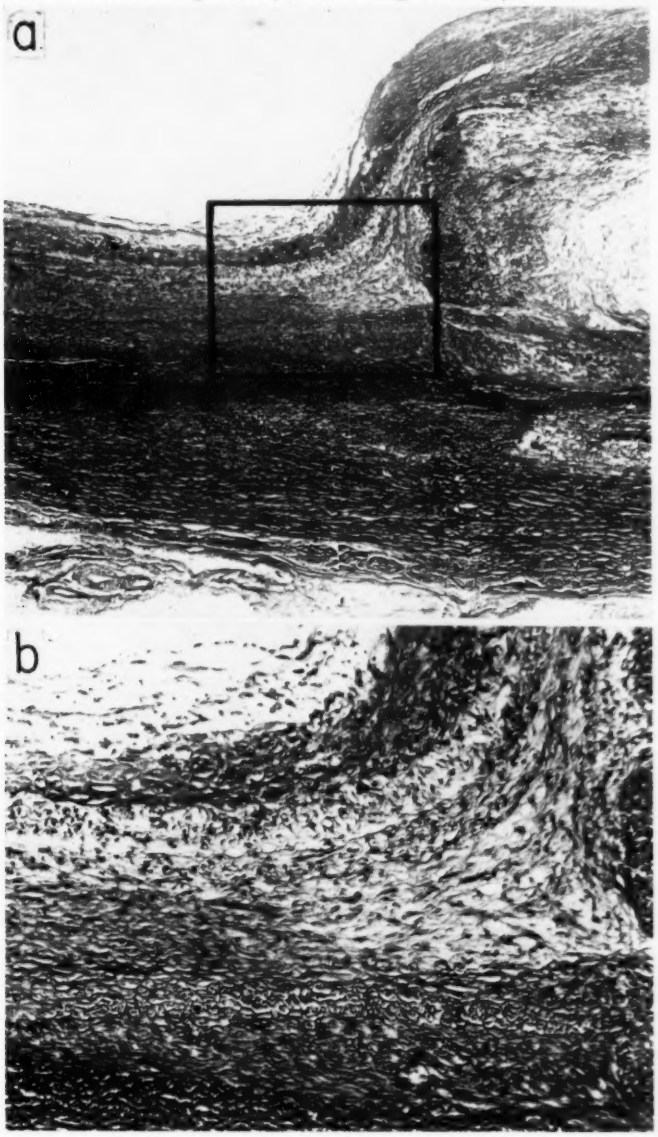


Fig. 1.—Abdominal aortic homograft after nine and three-fourths months of implantation into the abdominal aorta and after eight and three-fourths months of administration of cholesterol and radioactive iodine, with an average serum cholesterol level of 1,441 mg/100 ml. Note the massive atheromatous lesions, with an ulceration in the center of the graft. The host abdominal aorta was also markedly atheromatous, its proximal segment being more involved than the distal

moderate to very extensive. Usually the atheromatous lesions were more pronounced in its distal segment.

The graft was always the site of atheromatous degenerative changes (Fig. 1). The degree and extent of atherosclerotic lesions found in the graft ranged from small atheromatous plaques to involvement of its entire surface by degenerated atheromas with ulcerations and thrombus deposi-

Fig. 2.—Photomicrographs (*a* and *b*) of an abdominal aortic homograft after 12¼ months of implantation and after 11½ months of cholesterol and radioactive iodine administration. Note the subintimal plaque, consisting of fibroblastic connective tissue with abundant ground substance and occasional foam cells, especially in the superficial areas. Part of the plaque is markedly swollen, due to degenerative changes, with deposition of cholesterol crystals and precipitation of fibrin. Weigert elastica-Van Gieson stain; reduced to 85% of mag. × 40 (*a*) and of mag. × 125 (*b*).



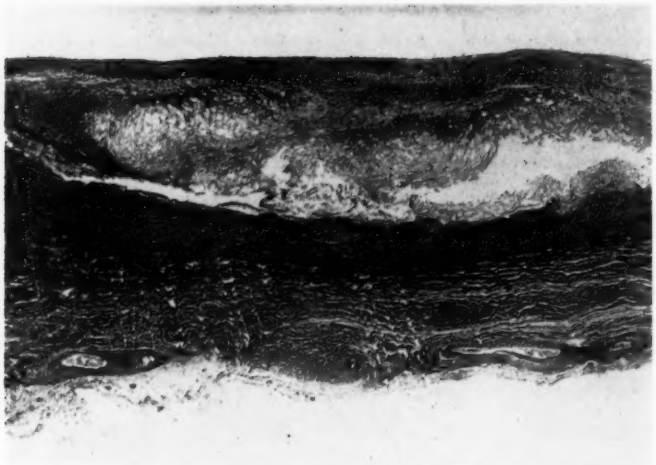
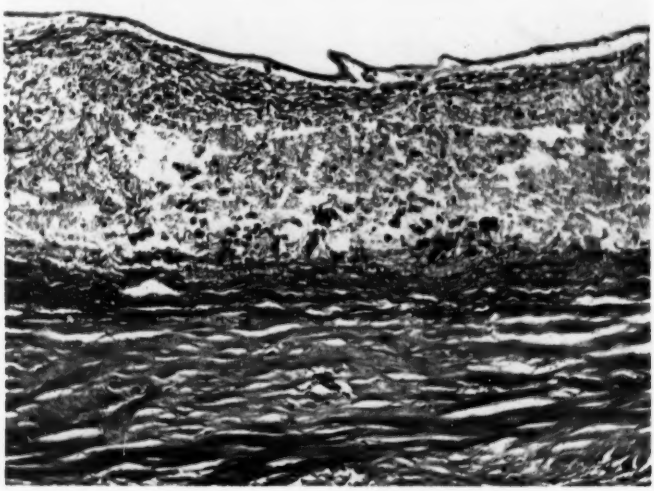


Fig. 3.—Photomicrograph of an abdominal aortic homograft, after four and one-fourth months of implantation and after four months of cholesterol-thiouracil administration. It shows a large subintimal plaque, consisting of fibrous tissue which has undergone atheromatous softening, with fragmentation of tissue and deposition of lipid material. Weigert elastica-Van Gieson stain; reduced to 60% of mag. × 40.

tions. Calcification of the graft and cleavage of its media were often encountered. As a rule the graft appeared to be more involved than the host abdominal aorta.

Histological sections of the graft showed intimal plaques composed predominantly of fibrous tissue proliferation with variable degrees of atheromatous degeneration (Figs. 2, 3). Foam cells were present in most of the intimal plaques. Calcification and chondroid changes were noted within the plaques in 3 of 12 cases (Fig. 4). In the area of anastomosis a thin intimal fibrous plaque was always present.

Fig. 4.—Photomicrograph of an abdominal aortic homograft, after six months of implantation and after five and three-fourths months of cholesterol-thiouracil administration. It shows a degenerated subintimal atheromatous plaque with calcific deposits. Hematoxylin-eosin stain; reduced to 85% of mag. × 125.



The inner layer of the media in the graft exhibited rather marked degenerative changes in most specimens. These changes consisted mainly in attenuation and separation of elastic fibers with swelling of the intervening ground substance. In severer forms they consisted in marked degenerative changes, with destruction or fragmentation of elastic fibers and abundant infiltration of foam cells. Occasionally, the degeneration was associated with calcification. The internal elastic membrane was usually intact, except in the presence of severe degenerative changes.

The host abdominal aorta exhibited intimal atheromatous lesions of variable degree, associated sometimes with marked degenerative lesions, to the point of liquefaction. In contrast with the lesions seen in the graft, the media of the host abdominal aorta showed less severe structural changes.

Enzymatic Studies

Succinic dehydrogenase and cytochrome oxidase systems were studied in slices of both graft and host aortic tissue. The oxidative capacity of these two enzymatic systems (Table 2), as expressed in cubic millimeters of oxygen per milligram of nitrogen per hour, showed the following average values for the graft and host abdominal aortas, respectively: 6.66 and 17.39 for succinic dehydrogenase and 8.75 and 16.75 for cytochrome oxidase.

Although the exact relationship between the oxidative capacity and the degree of atherosclerosis remains to be elucidated, the over-all biochemical data clearly indicate that the graft still exhibits a substantial degree of enzymatic activity, in spite of the marked degenerative changes described above.

Comment

In our previous series of experiments,[1] in which fresh thoracic aortic homografts were implanted into the abdominal aorta, the grafts exhibited only minimal or no atheromatous lesions. In contrast, in the present study, in which fresh abdominal aortic homografts were used, the implants showed consistently marked atheromatous alterations.

Predilection of the abdominal aorta for developing atherosclerosis is well recognized both in man[6] and in the dog.[1,7-9] Indeed, in both species the atheromatous lesions reach their greatest severity in the abdominal portion of the aorta. Reports by other investigators[7-9] and our own experience[1] clearly substantiate the observation that in the dog the abdominal aorta is susceptible to atherosclerosis, in contrast to the thoracic segment, which is largely refractory to it. Furthermore, the fact that thoracic aortic homografts implanted into the abdominal aorta, site of massive involvement in the dog, maintained the original refractoriness, whereas abdominal aortic homografts showed susceptibility to experi-

TABLE 2.—*Oxidative Capacity of Abdominal Aortic Homografts and Host Aortic Tissue of Dogs on Cholesterol-Thiouracil or Cholesterol-Radioactive Iodine Regimen*

Dog	No.	Homograft		Host Abdominal Aorta	
		$Q_{O_2}S$*	$Q_{O_2}PPD$†	$Q_{O_2}S$	$Q_{O_2}PPD$
1	912	9.55	9.53	14.35	12.83
2	918	2.93	3.95	11.49	11.11
3	921	14.40	14.06	19.90	10.96
4	923	6.63	6.10	25.75	22.25
5	926	1.08	4.77	12.66	15.75
6	933	2.27	16.75	14.40	21.80
7	936	10.00	7.48	24.36	25.19
8	937	6.44	7.33	16.18	14.25
	Average	6.66	8.75	17.39	16.75

* $Q_{O_2}S$ Oxygen consumption, in cubic millimeters per milligram of nitrogen per hour, using succinate as substrate.
† $Q_{O_2}PPD$ Oxygen consumption, in cubic millimeters per milligram of nitrogen per hour, using *p*-phenylenediamine as substrate.

mental atherosclerosis, would suggest an inherent biologic difference between the two aortic segments. The exact nature of this biologic difference remains to be elucidated.

Earlier studies on normal aortic tissue of the dog revealed that succinic dehydrogenase activity [2,3] and esterase activity [1] are markedly higher in the thoracic than in the abdominal segment. The role of these enzymatic findings with regard to their possible relationship to the susceptibility or lack of it to atherosclerosis is not entirely clear as yet. However, the difference in enzymatic make-up of the two aortic segments further underlines their biologic dissimilarity.

In this study, comparison of the oxidative capacity of the abdominal aortic homografts with that of the host abdominal aortic tissue indicates that both succinic dehydrogenase and cytochrome oxidase activities are diminished in the graft by about 60% and 50%, respectively. While a detailed analysis of their significance will appear elsewhere, these data indicate that the graft is enzymatically still active and is not a "dead" tissue, as the morphologic studies might have led one to believe.

Summary

Fresh abdominal aortic homografts were implanted into the abdominal aorta of 14 dogs subjected to a chronic cholesterol-thiouracil or cholesterol-radioactive iodine regimen. The fate of these grafts was studied by histological and biochemical methods.

Atheromatous lesions were present in variable degrees throughout the arterial system in all animals. The thoracic aorta was free of atherosclerosis in all but three cases. The host abdominal aorta was involved in 12 of 14 cases. The graft was always the site of atheromatous degenerative changes and, as a rule, appeared to be more involved than the host abdominal aorta.

Histological sections of the graft showed intimal plaques, composed predominantly of fibrous tissue proliferation, with variable degrees of atheromatous degeneration. Foam cells were present in most of the intimal plaques.

Study of the oxidative capacity of the graft showed that it still exhibited a substantial degree of enzymatic activity, in spite of the presence of marked degenerative changes.

Fresh abdominal aortic homografts showed marked susceptibility to experimental atherosclerosis, in contrast to fresh thoracic implants, which, as reported previously, remain largely refractory.

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DISCUSSION

DR. HARRIS B. SHUMACKER, Indianapolis: This interesting paper is now open for discussion.

DR. MICHAEL E. DE BAKEY, Houston, Texas: As Dr. Haimovici indicated, we, too, have been interested in this problem, and some of you may recall we published our results several years ago, using this method of producing arteriosclerosis in aortic homografts and in autografts and in controls, and we came to similar observations regarding the more frequent occurrence of arteriosclerosis in homografts. We also have published our observations on the use of this method in studying the occurrence of arteriosclerosis in synthetic grafts. It was reported at that time that these lesions failed to develop in synthetic grafts. Subsequent observations, however, showed that we were in error in reporting that they did not occur in the synthetic grafts. Since that time we have observed their occurrence in synthetic grafts. This error in observation resulted simply from lack of sufficient time. We had originally found that it was sufficient to allow from six months to a year for the great majority of the animals to demonstrate the occurrence of experimental arteriosclerosis, and within that period none of the animals in which the synthetic grafts had been used showed any evidence of arteriosclerosis. Fortunately, we kept some of these animals a little longer than a year, killing them from 13 up to 18 months, and some of them showed the typical arteriosclerotic lesions in the lining of the synthetic grafts. These observations, therefore, make it difficult to explain the occurrence of the lesions on the basis of a biologic inherent process within the graft.

DR. JOHN OLWIN, Chicago: I hesitate even to suggest a reason for the occurrence of arteriosclerosis in any of these grafts, but there has come to light recently some interesting work in connection with the possible relation of clotting to arteriosclerosis. We do not know what the role of lipoprotein lipase is in the metabolism of fats, but it is likely that it has some definite role. Thrombin has two activities that we know about. In addition to the clotting of fibrinogen, it also has an esterase activity; i. e. it will split the esterase linkage in certain substrates. And now it has recently come to light that thrombin will inhibit the action of lipoprotein lipase. Hence, excessive thrombin formation may inhibit the proper metabolism of fats by lipoprotein lipase and thus promote atheroma deposits. It is a straw in the wind, and I present it for your consideration.

DR. HENRY HAIMOVICI, New York: I wish to thank Dr. De Bakey and Dr. Olwin for their comments. Our experimental findings indicate a difference in susceptibility to atherosclerosis between the thoracic and the abdominal homografts. Although it may be premature to draw definite conclusions, the fact that thoracic aortic homografts when implanted into the abdominal aorta exhibited only minimal or no atheromatous lesions, while abdominal aortic implants showed consistently atheromatous alterations led us to the belief in the existence of an inherent biologic difference between the two aortic segments. The exact nature of this difference remains to be elucidated and is now under investigation. The difference in susceptibility of the two aortic homografts cannot be ascribed to a difference in duration of cholesterol administration. I wish to point out that in the series of thoracic aortic implants in which minimal or no atheromatous lesions were found, the duration of the atherogenic regimen ranged from 9 to 24 months, in contrast to the present series, in which the duration of the atherogenic regimen ranged from 4 to 12 months.

Study of Elasticized Dacron as Arterial Prosthesis

Experimental Comparison with Other Plastics, Homologous Arteries, and Autogenous Veins

W. ANDREW DALE, M.D., and F. N. NIGUIDULA, M.D., Rochester, N. Y.

Despite the widespread development of peripheral vascular shunt grafting for atherosclerosis of the femoropopliteal system, there is still no general agreement as to the best replacement material. Early enthusiasm for homologous arterial replacement appears to be waning as reports of degenerative changes in these grafts increase.[10,41] Difficulties in procurement of large numbers of arterial homografts have also proved to be a disadvantage as increasing numbers of patients seek operation. Autogenous vein grafts for peripheral vascular shunts have not developed wide surgical popularity, although recently there appears to be increasing approval of this material. The reluctant acceptance of veins may be due to the somewhat more difficult technique associated with their use and to some misunderstanding of the incidence of aneurysmal dilatation. This appears to be minimal when small peripheral veins are used as vascular replacements.[23] Aortic large-vessel replacement often results in aneurysm formation. A large number of synthetic prosthetic grafts have become available to date. Each of these has its advocates.

The reports of immediate postoperative clinical results far outnumber reports of careful long-term follow-up studies of experimental data. After Creech's editorial plea in 1955[5] for proper evaluation of synthetic prostheses, a committee was appointed by the Society for Vascular Surgery to compile available data, and this report was made in June, 1956, and published in January, 1957.[6] Data from 27 surgeons on 8 basic materials (17 different types) were analyzed, and 702 experimental aortic replacements were reported as 87% successful, whereas only 17% of 61 experimental peripheral prosthetic replacements were patent. Table 1 summarizes these and other reported experimental data on several previously or currently popular synthetics. From this it is seen that 83% (717 of 863) of the experimental aortic replacements were successful. Most of these grafts were 8 mm. or larger in internal diameter. Only 3% (1 of 32) of the grafts clearly defined as less than 8 mm. diameter and used peripherally remained open.* (The committee of the Society for Vascular Surgery reported that 44 of 96 experimental peripheral grafts remained open.) The success of the variety of aortic replacements, as well as the report of Harrison[19] (only 1 of 84 various thoracic aortic prostheses was thrombosed), indicates that aortic replacement is not a differential test of synthetic prostheses so far as patency is concerned. Experience in this laboratory with canine peripheral arterial shunt grafting using homologous arteries[28] and autogenous veins[23] suggest that the more difficult peripheral vascular replacement might serve to differentiate more critically between various grafting materials.

The present report compares the results of both central and peripheral prosthetic

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From the Department of Surgery, University of Rochester School of Medicine and Dentistry.

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* To avoid duplication, these figures omit those reported in each instance by the Society for Vascular Surgery Committee.

TABLE 1.—*Summary of Reported Experimental Results with Synthetic Vascular Grafts*

Reference	Position	I. D., Mm.	Length, Cm.	Patent/Total	Longest Period Followed, Days
	Vinyon-N				
Soc. Vasc. Surg. Comm. [6,9]	Aortic e-e			146/170	
	Peripheral art.			9/23	
Voorhees, Jaretzki, and Blakemore [44]					
Blakemore, and Voorhees [4]	Various		1-6	28/31	1,035
Griffith, Eade, Zech, and Harkins [14]	Thor. aorta (pigs)	10-13	3-7.5	12/14	
	Thor. aorta (pigs) †			16/18	
Shumacker and others [26]	Thor. aorta	8	5.4	10/16	600
	Nylon Fabric and Filter Fabric				
Soc. Vasc. Surg. Comm. [6]	Aorta			91/105	
	Peripheral art.			2/4	
Shumacker, Harris, and Siderys [30]	Abd. & thor. aorta ‡	6-10	4-10.8	51/65	310
Harrison [18]	Thor. aorta		308	27/28	
Self, Cooley, De Bakey, and Creech [27]	Thor. & abd. aorta §	7-11	1.5-2	6/10	196
Ouzounian [23]	Abd. aorta	7-12	2-5	10/10	100
Szilagyi, Shonnard, Lopez, and Smyth [42]	Aortic shunt	7.5-10	18-24	7/10 (3 stenotic)	195
Shumaker and others [24]	Thor. aorta	8	5.4	31/32	500
Barnett [3]	Abd. aorta	8	3-5	14/17	760
	Helanca Nylon				
Szilagyi, Whitcomb, and Shonnard [43]	Aortic shunt	7-10	13-15	14/14	365
	Crimped Nylon				
Soc. Vasc. Surg. Comm. [6]	Aorta			74/77	
Edwards and Tapp [12]	Abd. aorta	6.5	2	17/17	365
Shumacker and others [24]	Thor. aorta	8	5.4	14/15	400
Harrison [21]	Abd. aorta	8	5-6	7/11	180
Moore [19]	Thor. aorta		5	17/17	
	Dacron				
Soc. Vasc. Surg. Comm. [6]	Aorta			104/112	
	Peripheral art.			22/39	
Julian and others [15]	Thor. aorta ‖	10-13.7	5.5-10	21/21	365
	Abd. aorta ‖	6-10	4.5-11	27/32	352
Knox and Begg [16]	Abd. aorta	4		16/20	365
Pierpont and Blades [25]	Thor. aorta		4	8/8	180
Harrison [21]	Abd. aorta	6-8		12/26	
	Orlon				
Soc. Vasc. Surg. Comm. [6]	Aorta			28/37	
Hufnagel [17]	Abd. aorta ¶		5	90/95	180
Wesolowski and Sauvage [45]	Thor. aorta	10	6	11/12	181
	Abd. aorta (bifur.)	6	10	0/13	
	Orlon Knit				
Soc. Vasc. Surg. Comm. [6]	Aorta			30/30	
Sanger, Taylor, Matsuba, and Salomone [31]	Aorta			83 dogs satisfactory	
Harrison [19, 21]	Abd. aorta	8	5-6	10/15 (13 complicated)	180
	Ivalon				
Soc. Vasc. Surg. Comm. [6]	Aorta			36/41	
	Peripheral art.			11/30	
Mortensen and Grindlay [20]	Thor. & abd. aorta			17/17	330
McCaughan [24]	Thor. & abd. aorta	4-8	3	20/42	
	Thor. & abd. aorta	8-12		17/18	90
Martinez, Dahl, and Grindlay [27]	Abd. aorta		4-10	14/22	42
	Thor. aorta		6	0/8 (all ruptured or aneurysm)	186

TABLE 1.—*Summary of Reported Experimental Results with Synthetic Vascular Grafts* (Continued)

Reference	Position	I. D., Mm.	Length, Cm.	Patent/Total	Longest Period Followed, Days
	Vinyon-N				
Harrison [26, 21]	Abd. aorta	6-7	5-6	5/9 (2 ruptured or aneurysm)	189
Neville [21]	Aorta			21/25 (dilated or aneurysm)	730
Shumway, Gliedman, and Lewis [44]	Aorta			15/18	
Benjamin, Turbak, Hannon, Shumway, and Lewis [3]	Carotid & femoral	4-5	1-4.5	0/20	
	Teflon				
Soc. Vasc. Surg. Comm. [6]	Aorta			55/60	
Szilagyi, Shonnard, Lopez, and Smyth [47]	Aortic shunt	7.5-10	18-24	18/20	240
Harrison [16, 21]	Thor. aorta	9	6-7	18/18	
	Abd. aorta	6-8	5-6	28/30	
	Femoral & carotid	4	4	1/12	
Girvin, Schlosser, Eade, and Merendino [15]	Thor. aorta (pigs) †	11-20	3.1-7	9/10	293
Girvin, Wilhelm, and Merendino [16]	Thor. aorta	6-12	2.5-12	56/60	396

* Figures reported by the Committee for the Study of Vascular Protheses of the Society for Vascular Surgery undoubtedly includ[e] some of those listed below.

† Interposed arterial strip.

‡ Polyethylene or Lucite fused to nylon.

§ Braided nylon coated with vinyl.

‖ Ethicon's Ethi-Graft.

¶ Knit or sewn sheet Orlon.

vascular grafting (using several types) with homologous arterial and autogenous vein transplants in this laboratory. To date, this experience dictates our present use of autogenous veins for the majority of clinical peripheral shunt grafts (instead of the homologous arterial grafts, which were used until about a year ago), a prosthetic being the second choice for peripheral grafting and an homologous artery being the third choice.† On the other hand, synthetic materials have been the first, and essentially the only, choice for aortic grafting for approximately two years and have almost completely replaced the earlier use of arterial homografts in the aorta. The elasticized Fluflon Dacron prosthesis reported herein appears, on experimental grounds, to be an excellent grafting material on the basis of ease of suture, adaptability to its bed, nonkinking, proper porosity, and long-term patency characteristics.

† We are purposely omitting discussion of endarterectomy, which may be preferable for short blocks.

Methods

A series of 118 prosthetic grafts were placed in mongrel dogs with experimental conditions made as similar to clinical operations as possible. Operations were conducted under pentobarbital (Nembutal) anesthesia and respiration was sustained with room air under intermittent positive pressure whenever the chest was opened. Aseptic nonabsorbable (silk) suture technique was used. Antibiotics were not given except when a thoracotomy had been performed. No particular postoperative care was given to the animal or the wound.

Arteriograms were made at intervals, using sodium acetrizoate (Urokon sodium)‡ injected either percutaneously into the abdominal aorta or by a catheter threaded up into the aorta through the contralateral femoral artery.

Autopsy studies were limited to the grafted vessel and the immediately surrounding area. Sections were taken for microscopic studies.

Anastomotic technique consisted of over-and-over continuous 00000 silk ‡ sutures, interrupted at two points on the circumference of the stoma with mattress sutures. Shunts were performed in end-to-side fashion, so that the stoma diameter was approximately three times that of the lumen of

‡ Arterial silk was furnished by Ethicon, Inc., and acetrizoate (Urokon) by the Mallinckrodt Chemical Works.

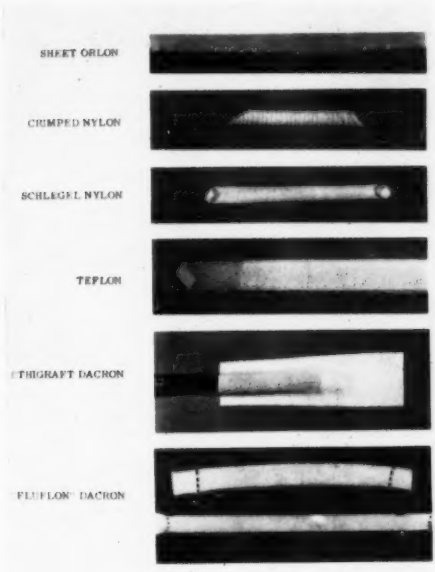


Fig. 1.—Samples of synthetic grafting materials used.

the host vessel. Heparinized saline (50 mg. of heparin in 200 cc. of saline) was used to wash out the host vessels after they were opened, but no general heparinization was used.

Synthetic prostheses were boiled in a detergent (Joy) solution for one hour and then washed well in tap water prior to autoclaving. Initially, these prostheses were not preclotted, but when it was realized that this process greatly decreased bleeding through the graft, preclotting became routine. At first this was done by simply soaking the graft in a pan of 10-20 cc. of fresh blood. Later it was found that intraluminal injection of this blood through the synthetic graft resulted in less bleeding. Figure 1 shows samples of the various prostheses. Fluflon Dacron prostheses § were cut to size with scissors. The end-to-end grafts had cuffs turned back prior to suturing. The end-to-side shunt grafts were cut squarely across and one end incised, so that a cuff was formed for most of the anastomosis (and so that each suture bite went through two layers of the cloth).

Crimped nylon prostheses § were cut and the ends lightly sealed by cautery. For shunt grafts a *V* was cut into one side to make a diagonally tapered end. Prior to placement each tube was stretched between the fingers to soften it and somewhat elongate its original form.

Teflon prostheses § were initially boiled in concentrated sulfuric acid for a week, at the end of which time the brownish discoloration due to various impurities had been completely removed by the acid, leaving a snow-white tube. End-to-end anastomoses were fashioned by incising each end of the tube to allow a short piece of material to be turned back on each side to make a flange about most of the circumference of the graft where it was sutured to the artery. At the ends of the incision, where there was no flange, a mattress suture was used. A modification of this technique was used for the end-to-side shunt grafts.

Ethi-Graft Dacron prostheses ‖ were cut to size by quickly passing a cautery across the ends. This also resulted in heat-sealing the ends, but they could be pried apart fairly easily. The projecting heat-sealed flanges of this graft prevented turning cuffs for the anastomoses.

Sheet Orlon prostheses were fashioned from large commercial-grade squares of Orlon cloth by forming a tube and suturing the edges together and turning cuffs.

Autogenous vein grafts were obtained at the time of operation by carefully dissecting out the saphenous vein of the animal and ligating its branches with 0000 silk. The vein was washed out with heparinized saline and reversed prior to placement so that the valves would point in the proper direction. Great care was taken to prevent intimal damage by instruments of any sort. Handling was done by picking up the adventitia or by cutting away portions which were handled at the ends.

The homologous arterial grafts were prepared (following a month's residence in the freezer but without drying) and placed for the most part by Mavor.[28]

Evaluation of Results

A total of 118 synthetic grafts were placed, with 105 animals surviving beyond the operative day, as shown by Table 2 and summarized in Table 3. Earlier deaths occurred chiefly in the thoracic aortic graft series prior to development of a temporary-pump bypassing technique, and these are not counted in any statistics. The individual experiments are summarized in Table 2,

§ Synthetic material was furnished as follows: Fluflon Dacron by Bentley, Harris Mfg., Conshohocken, Pa.; crimped nylon, by the Chemstrand Corp.; Schlegel nylon, by the Schlegel Manufacturing Co., and Teflon by John B. Sidlebotham, Inc., Philadelphia.

‖ "Ethi-Graft" Dacron was furnished by Ethicon, Inc., Somerville, N. J.

TABLE 2.—*One Hundred Five Synthetic Grafts in Dogs*

Dog No.	Position	Inside Diameter, Mm.	Length, Cm.	Days Patent (by X-Ray or Autopsy)	Autopsy Finding	Total Days Followed
			Fluflon Dacron			
57-408	Thor. abd. shunt	8	41	7	Patent graft, suture line leak	7
58-265	Thor. aorta e-e	16	6.5	1 & w	Patent graft	14
58-175	Thor. aorta e-e	8	6	1 & w	Patent graft	60
58-218	Thor. aorta e-e	16	6	3	Patent graft, died pneumonia	3
58-221	Thor. aorta e-e	16	6	8	Patent graft, suture line leak	8
57-19	Abd. aorta e-e	8	6.5	310	Patent graft	310
57-7	Abd. aorta e-e	8	5.2	462	Patent graft	462
56-529	Abd. aorta e-e	8	5.3	455	Patent graft	455
57-23	Abd. aorta e-e	8	6.7	77	Patent graft, Urokon paralysis	77
57-79	Abd. aorta e-e	8	7.5	426	Patent graft	426
56-528	Abd. aorta e-e	8	6.5	21	Patent graft, aneurysm proximal	21
57-365	Aortoiliac shunt	8	10	34	Patent graft	34
57-Z	Aortoiliac shunt	8	9.5	170	Patent graft	170
57-418	Aortoiliac shunt	8	9	186	Patent graft	186
57-416	Aortoiliac shunt	6	9	175	Patent graft	175
57-446	Aortoiliac shunt	8	9	49	Thrombosed graft	182
57-438	Aortoiliac shunt	6	8	43	Thrombosed graft	176
57-462	Aortoiliac shunt	8	8	168	Patent graft	168
57-485	Aortoiliac shunt	8	8.5	161	Patent graft	161
57-370	Aortoiliac shunt	8	9	0	Thrombosed graft	102
57-452	Aortoiliac shunt	6	8	0	Distal graft thrombosed	58
57-262R	Femoral shunt		10	45	Patent graft	45
57-244R	Femoral shunt	4	11.5	215	Thrombosed graft	334
57-244L	Femoral shunt	4	10.7	215	Thrombosed graft	334
57-122R	Femoral shunt	6	10	27	Thrombosed graft	136
57-122L	Femoral shunt	6	9	27	Thrombosed graft	136
57-262L	Femoral shunt		10	0	Thrombosed graft	45
57-284R	Femoral shunt	4	7	0	Both anastomoses blocked	67
57-284L	Femoral shunt	4	6.5	0	Both anastomoses blocked	67
57-119	Femoral shunt		11	0	Distal anastomoses blocked	24
57-166R	Femoral shunt	6	10	0	Both anastomoses blocked	97
57-166L	Femoral shunt	4	9.7	0	Both anastomoses blocked	97
57-245	Femoral shunt	4	8	0	Thrombosed graft	47
			(Edwards-Tapp) Crimped Nylon			
57-188	Thoracic to abdominal aortic shunt	8	23	302	Patent graft, distal anas. narrow	302
57-243	Thoracic to abdominal aortic shunt	8		336	Patent graft	336
57-233	Thoracic to abdominal aortic shunt	8	30	7	Patent graft, diaph. incarc. stomach	7
57-194	Thoracic to abdominal aortic shunt	8		1	Patent graft, diaph. incarc. stomach	1
57-255	Thoracic to abdominal aortic shunt	8		2	Patent graft, (?) cause death	2
58-165	Abd. aortic e-e	8	6			
58-146	Abd. aortic e-e	8	6			
56-138	Aortic e-e	9.5	5	532	Patent graft	532
56-250	Aortic e-e	9.5	5.5	501	Patent graft	501
56-24	Aortic e-e	9.5	5	534	Patent graft	534
57-304	Aortic e-e	8	5	273	Patent graft	273
56-112	Aortic e-e	9.5	5.5	163	Prox. anastomoses blocked	281
56-465	Aortic e-e	9.5	6	0	Fibrous clot both anastomoses	135
56-471	Aortic e-e	9.5	6	0	Prox. anastomosis occluded	87
56-260	Aortic e-e	9.5	6	0	Central thrombosis of graft	83
56-459	Aortic e-e	9.5	5	0	Both anastomoses blocked	42
55-373	Aortoiliac shunt	9.5	4	755	Patent graft	755
56-267	Aortoiliac shunt	9.5		545	Patent graft	545
56-454	Aortoiliac shunt	8	9	407	Patent graft	407
55-307L	Aortoiliac shunt	8	4.5	732	Patent graft	732
55-307R	Aortoiliac shunt	8		0	Thrombosed graft	732
56-138	Aortoiliac shunt	9	6	0	Thrombosed anastomosis	60

56-286	Aortoiliac shunt	8	6.5	0	Thrombosed anastomosis	88
56-28	Aortoiliac shunt	8	12	0	Thrombosed graft	90
56-500	Aortoiliac shunt	8	7.5	0	Thrombosed anastomosis	69
55-430	Iliofemoral shunt	8	12	0	Thrombosed graft	78
55-509	Iliofemoral shunt	8		0	Thrombosed graft	73
56-78	Iliofemoral shunt	8		0	Thrombosed graft	63
56-68	Iliofemoral shunt	8		46	Thrombosed anastomosis	200
56-103	Iliofemoral shunt	8		39	Thrombosed proximal anastomosis	197
56-49	Iliofemoral shunt	8	14	0	Thrombosed graft	137
56-82	Iliofemoral shunt	8		0	Thrombosed graft	60
56-115	Iliofemoral shunt	8	16	0	Thrombosed anastomosis	104
56-120	Iliofemoral shunt	8	15	0	Thrombosed graft	38
56-410	Femoral shunt	8		47	Both anastomoses fibrosed	137
56-497	Femoral shunt	8	8	0	Both anastomoses fibrosed	62
56-515	Femoral shunt	8	9	17	Patent graft, died distemper	17
56-527	Femoral shunt	8	10	0	Both anastomoses occluded	48
57-8	Femoral shunt	8	9	0	Both anastomoses occluded	45
			Schlegel Nylon			
56-331	Abd. aortic e-e	7	5.5	390	Patent graft	390
56-342	Abd. aortic e-e	7	4.5	370	Patent graft	370
56-483	Abd. aortic e-e	7	6	298	Patent graft	298
56-367	Abd. aortic e-e	7	5	2	Patent graft, (?) cause death	2
55-487	Abd. aortic e-e	7	6	89	Thrombosed graft	111
56-363	Abd. aortic e-e	7	5	1	Small clot at anas.; (?) cause death	1
56-388	Abd. aortic e-e	7	6	20	Fibrous clot prox. anas.; (?) cause death	193
56-15	Femoral shunt	6	5	539	Patent graft	539
56-71	Femoral shunt	6	5	486	Patent graft	486
56-101	Femoral shunt	6	6	419	Patent graft	419
56-134	Femoral shunt	6	6	22	Patent graft; died distemper	22
55-480	Femoral shunt	6	5	33	Thrombosed graft	189
55-501	Femoral shunt	6	4.3	0	Thrombosed graft	111
55-492	Femoral shunt	6	4.5	0	Thrombosed graft	105
56-67	Femoral shunt	6	5	0	Thrombosed graft	83
56-30	Femoral shunt	6	5	0	Infected, thrombosed at autopsy	84
56-81	Femoral shunt	6	6	0	Thrombosed graft	31
56-113	Femoral shunt	6	5.5	0	Thrombosed graft	47
			Teflon			
56-117	Aortic bifurcation	9-6.5		0	Thrombosed graft	75
57-56	Aortic e-e	7.6	8	0	Thrombosed graft	42
57-88	Femoral shunt	5.1	10	16	Patent with severe anas. constriction	16
57-77	Femoral shunt	5.1	10	0	Thrombosed graft	29
57-72	Femoral shunt	5.1	10	0	Thrombosed graft	24
57-93	Femoral shunt	5.1	10	0	Thrombosed graft	24
57-117	Femoral shunt	7	10.5	0	Thrombosed graft	42
57-115	Femoral shunt	5.1	10	0	Thrombosed graft	74
			(Ethicon) Dacron			
57-263	Aortoiliac shunt	6.7		205	Patent graft	205
57-457	Aortoiliac shunt	8	9	157	Patent graft	157
57-468	Aortoiliac shunt	8	10	93	Patent graft	93
57-454	Aortoiliac shunt	8	10	0	Prox. anastomosis fibrotic	60
			Sheet Orlon			
55-508	Femoral shunt	6		0	Anas. occluded, graft empty	94
56-12	Femoral shunt		4	0	Thrombosed graft	8
55-484	Aortic e-e		3	0	Thrombosed graft	12

TABLE 3.—*Summary of 118 Synthetic Grafts in Dogs*

Material	Survivors	Died	Total	End-to-End			Shunts			Open/ Total *
				Thoracic Aorta	Abdominal Aorta	Thor. to Abd. Aorta	Aortoiliac	Iliofemoral	Femoral	
Fluflon Dacron	33	5	38	4/4	6/6	1/1	6/10		1/12	18/33
Crimped nylon	39	6	45		6/11	5/5	4/9	0/9	1/5	16/39
Schlegel nylon	18	2	20		4/7				4/11	8/18
Teflon	8	0	8		0/2				1/6	1/8
Ethi-Graft Dacron	4	0	4				3/4			3/4
Sheet Orlon	3	0	3		0/1				0/2	0/3
Total	105	13	118	4/4	16/27	6/6	13/23	0/9	7/36	46/105
% Patent				100%	59%	100%	57%	0%	19%	44%

* The ratio 18/33 represents 18 grafts patent at death in a total of 33 dogs.

where the total postoperative time prior to killing the animal is given in the last column and where the proved graft-patency time is shown in the fifth column. For example, Dog 55-487 (Schlegel nylon, abdominal aorta end-to-end) showed a patent graft by aortogram at 89 days but thrombosis at 111 days, because of which he was killed. A summary of these results appears as Table 3.

Fluflon Dacron proved to be the easiest material of all to handle and use as a graft. It is produced from a Dacron yarn which is twisted at high speed while being heated to produce a crinkly fiber and braided into a two-way stretch tubing. Figure 2 is a magnified view of Fluflon Dacron, emphasizing the twisted, coiled fibers. Because of its lateral elasticity (Fig. 3), a cuff is easily turned without wrinkling the tube. This eliminates the need for heat-sealing the ends and allows sutures to bite a double thickness of the tubing. This two-way stretch appears to offer an advantage over one-way longitudinal-stretch Dacron tubes reported earlier. The method of cutting the end square, slitting one side, and turning the edges back as flanges for an end-to-side anastomosis is shown by Figure 4A. The brisk bleeding through pores which occurred if Fluflon Dacron was not preclotted could be easily prevented by injecting 20 cc. of blood through the tube three or four

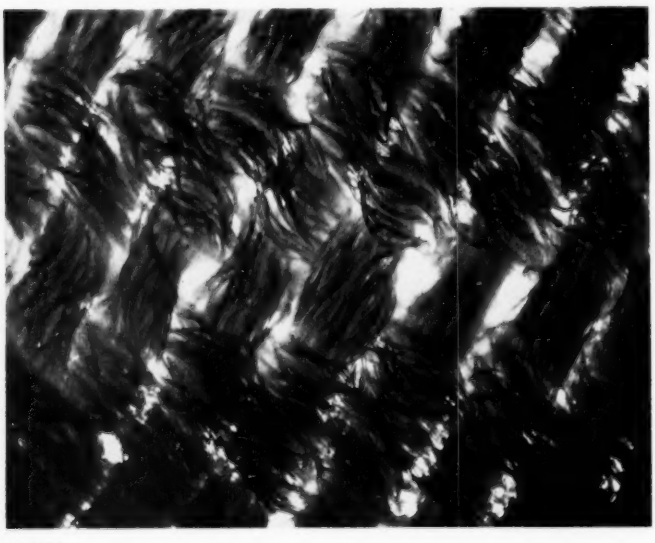


Fig. 2.—Photomicrograph of Fluflon Dacron.

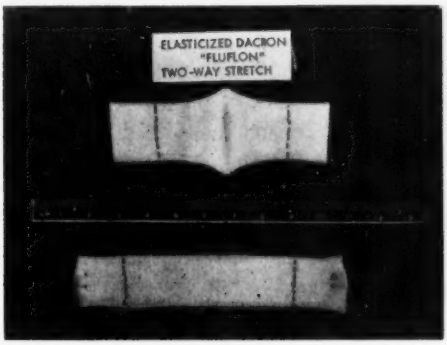


Fig. 3.—Fluflon Dacron stretches in two directions. The two tubes are of the same dimensions, with the upper stretched laterally and the lower longitudinally.

times prior to placement. Figure 4 shows such a prosthetic graft placed as a femoral shunt graft in a dog.

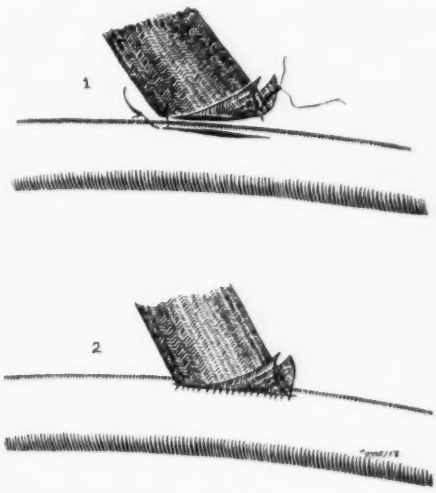
Experience with Fluflon Dacron as a thoracoabdominal shunt and as a thoracic aortic end-to-end graft was marred by many early deaths. The immediate fatalities do not appear in Table 2. (Why two of the four survivors should die at seven and eight days of suture-line leaks is unknown, since such did not occur at any other time.) The grafts appeared patent. All six abdominal aortic grafts also were patent.

There were 6 of 10 aortoiliac shunt grafts, but only 1 of 12 femoral shunt grafts, which remained patent. The low patency rate associated with 4 and 6 mm. inside diameters of the tubes placed as femoral shunts has occurred with all types of synthetics, but not in such high percentage with homologous arteries or autogenous veins.

Gross examination of the grafts showed infiltration of the synthetic material by granulation and later fibrous tissue, with gradual lining of the graft by a smooth "neointima" (Fig. 5). Delay in completion of this lining was seen in all types from time to time. Microscopic analysis did not particularly differentiate the responses of the tissues among the several plastics. Fluflon Dacron is tolerated, infiltrated, and lined as are other synthetics, as illustrated by Figure 6.

Edwards-Tapp crimped nylon tubes[12] were placed in 39 dogs, as indicated in Tables 2 and 3. In the majority of these tubes the inside diameter was 8 mm., although one was as small as 5 mm. and a few were as large as 9.5 mm. At death, 16 of the 39 tubes were patent. In five dogs 8 mm. tubes were placed as successful shunts between the thoracic and the abdominal aorta, (five other dogs died too early to be counted); three of these five died in

Fig. 4.—Fluflon Dacron shunt graft in femoral artery of dog at conclusion of operation. Fig. 4A. —Tube is split along one side to allow a flange to be turned on each side.



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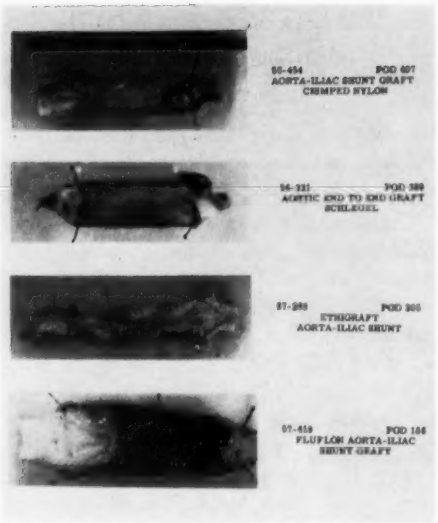

Fig. 5.—Autopsy specimens of four types of synthetic grafts. The neointima is similar in all.

the early postoperative period of factors unrelated to the graft itself, while two survived for a long time. Only 6 of 11 dogs with aortic end-to-end grafts survived with patency for a long period. However, of the five grafts which failed to remain patent, it was noted that four showed anastomotic constriction with an essentially empty graft. Nine aortoiliac shunt grafts of crimped nylon were placed, with one early death of unknown cause, but probably related to postoperative shock, and with four grafts remaining patent for a long period. Crimped nylon grafts of similar diameter placed between the iliac and femoral arteries so that they coursed beneath the inguinal ligament became thrombosed 100%. Since these operations were done with essentially the same technique and essentially the same previous experience as the aortoiliac shunts, the difference suggested that the constricting effect of the inguinal ligament caused a higher incidence of thrombosis, and that position was not used further. Of the five femorofemoral shunts, only one was patent, and that on the 17th postoperative day, when the animal died of distemper. The other four had notable fibrosis of both anastomoses, probably due to the difficulty of suturing an 8 mm. graft to the tiny femoral artery of moderate-sized dogs. Experience with these 39 crimped nylon grafts indicated the extreme care which must be taken with cutting and heat-sealing the ends to prevent inward protrusion of nylon fibers at the anastomotic lines. Even with proper heat-sealing there was often a tendency toward fraying of the ends, particularly if instrumental handling was

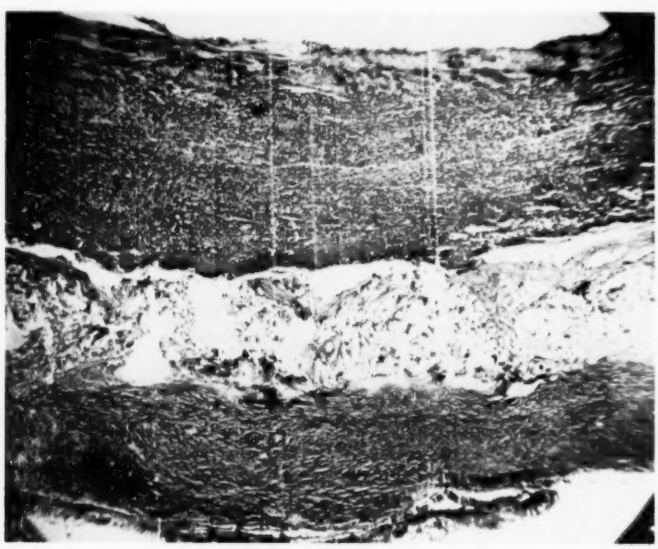

Fig. 6. — Photomicrograph of autopsy specimen of Fluflon Dacron prosthesis. The neointima (above central synthetic) is thicker than the wall of the Dacron tube.

done at any time. This has also been noted in clinical cases. While there was considerable blood loss through the crimped nylon prostheses, which were inserted prior to preclotting, this was well controlled once the preclotting technique was adopted.

Schlegel seamless woven nylon tubes were placed as aortic end-to-end grafts in seven animals, of which four survived with patent grafts. The two dogs which died, on the first and second postoperative days, respectively, had grafts that were still patent. These were all 7 mm. in diameter. Eleven Schlegel grafts of 6 mm. inside diameter were placed as femorofemoral shunts, with four grafts patent at autopsy. One of the four dogs with patent graft died at 22 days, with distemper, leaving a corrected figure of 3 in 10. The stiffness of this tube and the increasing availability of other tubes led to cessation of further attempts with this particular material.¶

Woven Teflon tubes were placed in eight dogs. Both the aortic replacements became thrombosed, and all except one of the femorofemoral shunt grafts was thrombosed. The single dog with patent graft was killed at 16 days, and the graft was found to have a severe anastomotic constriction, indicating that it probably would have become thrombosed later. The small size of these tubes (5.1 mm.) no doubt ruled against their success. They were also difficult to handle and to suture and tended to wrinkle. (A newer type of crimped Teflon may not be so difficult to use but has not yet been evaluated.)

Dacron tubes (Ethi-Graft) were placed as aortoiliac shunts in four animals after this flanged sealed tubing became available. Three animals were killed with patent grafts, while the fourth was killed at 60 days with a fibrotic proximal anastomosis. The chief disadvantage of the straight Dacron tubes which were used in these experiments was the difficulty, after cutting it diagonally, in suturing it as an end-to-side shunt graft, as well as in handling the flanges.

Sheet Orlon was sewn into tubes and placed as femoral shunt grafts twice and once as an aortic end-to-end graft early in our experience. All were thrombosed. In retrospect, it is recognized that these tubes were crude fabrications and probably had little chance of remaining patent.

Comment

The above-detailed experimental grafting procedures not only confirm the belief that peripheral vascular grafting in dogs is associated with a greater likelihood of thrombosis than is aortic grafting but also point up the advantages and disadvantages of various synthetics much more clearly than does aortic replacement. For instance, while it may be possible to place a stiff-walled, nonpliable piece of material into the abdominal aorta, undesirable characteristics are immediately emphasized by attempting to graft a smaller tube of similar material into the iliofemoral system. Similarly, whereas an aortic replacement may function even though there is protrusion of some of the fibers across the suture line into the lumen, this will usually cause immediate thrombosis in a more peripheral graft. Thus peripheral grafting in dogs is a severer test than is aortic replacement. While the immediate deposition of fibrin and the thickness of the pseudointima covering a synthetic may prevent excellent results from often being achieved in the peripheral position in dogs, it is known, on the basis of our previous arterial and venous transplantations, that these small vessels can be grafted if the proper material and technique are used.

The synthetics used in this series were selected from time to time from the large group which has become available. Since it was impossible to test all, the materials used were selected initially on the basis of the descriptions of other workers or because of certain characteristics which appeared to be desirable.

¶ Many of the actual operations with Schlegel nylon were performed by Dr. Raymond Hinshaw.

TABLE 4.—*Evaluation of Small-Graft (from Aorta, Iliac, or Femoral Artery to Distal Femoral Artery) Patency in This Laboratory*

Graft Material	Patent/Total	Per Cent Patent
Homologous artery [28]	31/39	80
Autogenous vein [23]	24/28	86 *
Various prostheses	20/68	30

* Parenthetical vein percentage explained as adjusted in text.

Table 4 compares the results of the arterial, venous, and synthetic grafts to small peripheral dog vessels in this laboratory. Eighty per cent of the homologous arteries remained patent a minimum of three weeks.[28] Eighty-six per cent of the autogenous vein shunts remained patent.[23] (This figure omits failures while one is learning the more difficult technique of handling veins.) The patency rate for the 68 various prosthetic shunts from aorta, iliac, or femoral artery to a distal vessel was only 30%, despite the fact that these operations were done after the artery and vein work and so should have led to a better synthetic graft technique. Since 32% (7/22) of the Fluflon Dacron, 26% (5/19) of crimped nylon, 36% (4/11) of Schlegel nylon, and 17% (1/6) of Teflon tubes remained patent in small dog vessels, there seemed little reason to choose one over another from the standpoint of experimental patency results. All, however, are less successful than homologous arteries or autogenous veins.

Fluflon Dacron has certain advantages over the other materials tested which suggest it for further experimental evaluation and for early clinical evaluation, although these advantages do not include a higher patency rate. Its ease of suture and handling recommends it, and these animal experiments appear to indicate that the prosthesis will remain patent when placed as a small vessel graft as well as any of the other materials tested. The two-way-stretch characteristic seems of some importance, because, unless there is lateral elasticity, a cuff must necessarily result in some wrinkling of the inner layer. The possibility of turning a cuff of Fluflon Dacron allows a smooth end and a firm edge for suturing, without the necessity of sealing fibers by heat which occurs with crimped nylon in particular. With the technique illustrated in Figure 4A, such a flange can also be turned when an end-to-side shunt graft is placed. The elasticity also allows the elasticized Dacron prosthesis to readily adapt itself to its bed. While the pulsation through the graft immediately after placement is attractive to the surgeon, it appears doubtful that this is of any importance in itself, because the elasticity disappears within a short time, as a result of fibrous tissue infiltration.

While it has been stated that synthetic grafts cause loss of pulse pressure distally,[36] our experience indicates that such loss is the result of a faulty anastomosis or of a clot within the graft, rather than of any characteristic of the synthetic material itself.[32] Figure 7 shows the proximal and distal pulse pressure records for a dog with an aortoiliac Fluflon Dacron prosthetic shunt. This and Table 5 (five studies of Fluflon Dacron pulse pressure transmission) indicate no loss of pulse characteristics due to the graft, even in the later postoperative period, after fibrous tissue

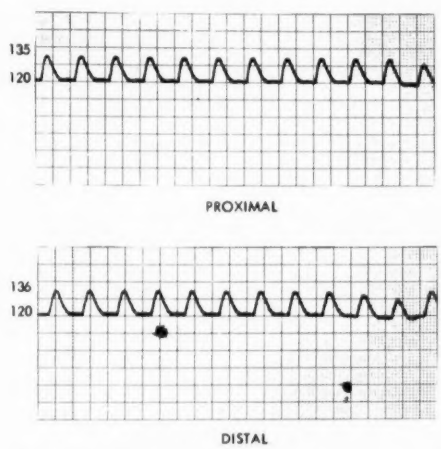

Fig. 7.—Pulse-pressure tracings both proximal and distal to a Fluflon Dacron aortoiliac shunt graft show no decrease.

TABLE 5.—*Five Studies of Pulse Pressure Proximal and Distal to Aortic-Iliac Shunt Grafts of Fluflon Dacron*

Dog	P. O. Day	I.D., Mm.	Length, Cm.	Pulse Pressure, Mm. Proximal	Distal	Difference
57-Z	170	8	9.5	13	11	− 2
57-416	175	6	9	36	48	+12
57-418	186	8	9	28	28	0
57-485	161	8	8.5	30	30	0
57-462	168	8	8	16	20	+ 4

infiltration has occurred. The same is true of all other plastics used by us, so long as the anastomoses are correct. Failure of a graft to transmit a good pulse should at once be interpreted as indicative of technical error or clotting.

The poor results of synthetics as compared with either homologous arteries or autogenous veins in the peripheral vascular system of these dogs prompts us to reserve synthetic tubes as a secondary material for use in small vessels of patients. Our good experimental experience with autogenous veins reported to this Society a year ago[23] has been confirmed in clinical usage in over 20 patients over the past year. The technique of vein grafting has proved to be a more delicate one, but excellent early results have been obtained in these initial patients, so that autogenous veins have replaced homologous arteries as the material of clinical choice for peripheral grafting here. The later degenerative changes in small homologous arterial grafts here, as well as elsewhere,[10,41] have relegated this material to third place for peripheral human grafting and has led us to prefer a synthetic tube to "back-stop" the autogenous vein if that should not be available or usable. These experiments do not clearly indicate that any of several synthetics is best for small vessels in term of long-term patency, but does show that Fluflon Dacron is initially the easiest to handle technically and performs as well as any other in the later postoperative period. Its early clinical trial is in order.

Summary

The results of 118 synthetic arterial grafts placed in various positions in dogs indicate the considerably greater risk of occlusion in small peripheral vessels than in central vessels, such as the aorta. The canine peripheral vessel thus becomes a severer test of a grafting material. Only 30% of 68 synthetic grafts of various types remained patent in canine peripheral vessels, whereas previous experience here indicated that 80% of homologous arteries and 86% of autogenous veins remained patent. This has led to our clinical preference for the autogenous vein as the primary peripheral replacement in patients. Fluflon Dacron proved to be the easiest synthetic graft to handle and remained patent as well as any of the other synthetics used in these experiments. It sutures well, adapts itself to the bed, and carries a pulse well. It is proposed that such material be used clinically to graft peripheral vessels when autogenous veins are not usable.

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DISCUSSION

Dr. D. E. Szilagyi, Detroit: I would like to stress one point. I do not believe that the rate of early thrombosis is a very satisfactory criterion by which to evaluate the performance of an experimental graft, especially when the graft is inserted in the peripheral artery of a dog, where the technical problems of anastomosis are so great. The technical difficulties in such a situation may overshadow other important variables, and in effect one may be testing one's technical skill rather than the behavior of the implant. It is my belief that, when inserted under appropriate conditions, a number of plastic protheses will give similar, good early-patency rates, and that their respective merits will lie not in this quality but, rather, in the arteriogenesis they elicit and in the persistence of their tensile strength. The type of Dacron used in the elastic Dacron prostheses we have reported on has shown most satisfactory results from these points of view during a period of 18 months. It should be made clear that the Dacron tubing Dr. Dale has described is a different product. We carried out a few experiments with this type of Dacron prosthesis about three years ago and found that in 12 months it had lost 90% of its tensile strength.

Dr. Denton A. Cooley, Houston, Texas: I would like to present some of our own experience with a new vascular substitute which was developed at Baylor in cooperation with the Philadelphia Textile Institute. The graft is a crimped, knitted Dacron tube, which can be cut with scissors without fraying the ends. In our experience these tubes have been superior to homografts and other types of vascular substitutes, including the synthetic materials. One obvious difference has been the greater strength of the Dacron tubes as compared with that of homografts. Seldom does one have a postoperative hemorrhage which was not a rare complication of homograft replacements. Dacron tubes appear to resist infection, and thus secondary hemorrhage is prevented.

In our series of 500 cases of vascular graft using the Dacron grafts, 22 deaths occurred, with 17 graft failures. Our own experience with homografts was not this good, and I doubt whether any experimental evidence at this time would influence us to change back to homografts. Of course, the practical advantage of the synthetic grafts is obvious.

Dr. W. Andrew Dale, Nashville, Tenn.: I should like to thank Dr. Szilagyi and Dr. Cooley for their comments. Actually, our experiments do not indicate that any one synthetic is better than others but that for small-vessel replacement autogenous veins are more apt to be successful than are any of the synthetics. Successful replacement of the small canine vessels indicates that such can be used to evaluate various graft materials.

Dacron Tube and Bifurcation Arterial Prostheses Produced to Specification

II. Continued Clinical Use and the Addition of Microcrimping

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There is an increasing acceptance of synthetics as desirable substitutes for preserved homologous arteries in vascular surgery. This is due to the difficulties which are reported with homografts as experience becomes greater. It is fortunate that the severe progressive deterioration of tissue grafts often observed in experimental animals [1] has been recognized infrequently in man. On rare occasions host reaction has led to rapid and severe inflammatory changes in and about homologous arteries after transplantation. More gradual changes include thrombosis, aneurysm, and scar-tissue constriction. An exaggerated tendency of the grafted vessel to participate in the atherosclerotic process of the patient has been described.[2] Even though the present data indicate a satisfactory experience with one of the synthetics, it is reasonable to emphasize that a long-term experience with synthetics comparable to that which is now revealing defects in homologous arteries may at sometime in the future indicate disadvantages of synthetic grafts which will be equally important.

Considerable evidence has accumulated indicating the relative inertness of a number of plastic-fabric prostheses. Since the original contribution of Voorhees, Jaretzki, and Blakemore,[3] the lasting qualities of certain synthetic materials have repeatedly been observed. A variety of materials have been used in clinical vascular surgery after testing in experimental animals. Vinyon-N, which was found satisfactory by Voorhees et al., was followed in rapid succession by nylon, Orlon, Dacron, and Teflon. Most of these materials have been found sufficiently inert, lasting, and low in production of undesirable tissue reaction. However, on a comparative basis, the degree to which various substances exhibit these factors has favored Dacron and Teflon. Therefore, most of the recent prostheses commercially developed have been of these materials.

Emphasis rightly has been placed on the method of construction of artificial vascular prostheses utilizing these materials. Initially, flat fabrics seamed on a sewing machine were used in the form of large tubes and bifurcations. They proved so laborious, and at times insecure, that other methods of construction were sought. Woven, knitted, or braided seamless tubes used either flat or after crimping have presented certain real advantages. This has been at the expense of increased thickness and lessened flexibility in the braided or knitted tubes.

In 1956 we [4] described a method of making woven tubes and bifurcations of Dacron.* These prostheses were produced by a duplication weaving process in which two layers of taffeta Dacron cloth were woven simultaneously on a single loom, the layers

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* Also known as Mersilene.

being joined together by the crossing of the yarn along predetermined outlines. A variety of sizes and shapes of bifurcations and straight or curved-end tubes were produced. The various forms which were cut from the fabric matrix provided flat prostheses, which were essentially seamless internally.

In the previous report certain advantages and disadvantages of these prostheses were presented. In brief, it was found that a readily available standard pattern in various sizes was satisfactory for replacement of the aortic bifurcation or the descending thoracic aorta after aneurysm resection. The junction of the two fabric layers was found to be extremely strong. The lack of thickness and bulk of the implant was thought to be desirable.

As in all synthetic prostheses currently used for vascular replacement without additional coating, calendering, or other treatment, these grafts required, and continue to require, preclotting. They shared with other porous materials the disadvantage of a variable degree of initial blood loss in spite of preclotting.

The principal disadvantage of this method of construction appeared in the use of the prosthesis as a flat tube, especially for femoral bypass grafts. Whereas the aortic replacements were found to be sufficiently satisfactory for continued use, the straight tubes were awkward to handle. A 50% early failure rate was observed clinically in the initial report, and experimentally the straight tubes showed a 20% failure rate in the aorta of dogs. Some of these deficiencies arose from the inability of the graft to curve without kinking. It was observed that when flat tubes were produced with curved ends, the failure rate in dogs was much less and clinical application more successful. This tendency to kink, however, limited the clinical use of these grafts to bypasses confined entirely within the thigh. It was not possible to retain a good success rate if the graft traversed either the inguinal fold or the popliteal space. An inadequate bypass of diseased vessels resulted, and some of the thrombotic failures occurred because adequate run-off levels were not reached.

TABLE 1.—*Dacron Bifurcations*

		Univ. Illinois	Columbia P. & S.
First series	Aneurysm	11	3
	Rupt. aneurysm	2	2
	Leriche syndrome	2	0
	Mortality	3	2
	Late failure	0	0
Present series	Aneurysm	45	12
	Rupt. aneurysm	10	0
	Lerichery	0	0
	Mortality	7	1
	Late failure	0	0
	Total grafts	87	
	Mortality	13 (14.8%)	

Improvement has been sought in several directions. It is the purpose of this report to present (1) additional data concerning the present longer follow-up period in the group of cases reported previously; (2) changes in the structure of the bifurcations and the results in use of bifurcations in an enlarged series in aneurysm replacement, and (3) production, animal testing, and clinical results of the use of a microcrimped version of the woven prostheses.†

Clinical Use of Flat Woven Dacron Bifurcations

A total of 87 flat taffeta Dacron bifurcations have been implanted (Table 1). The series includes use of the bifurcation in resectional therapy of 85 abdominal aortic aneurysms. Of these bifurcations, 12 were used during resection of ruptured aneurysms and 73 in elective resections. In the group of ruptured aneurysms there was a mortality of six patients, and in the elective resections there was a surgical mortality of seven patients. In addition, one patient died one year postoperatively as a result of coronary occlusion, and one, three months postoperatively, owing to rupture into the jejunum of a pulsating hematoma at the proximal anastomosis. Implantations in the abdominal aorta following resection

† Available from Ethicon Inc., Somerville, N. J.

of aneurysms have now been followed a maximum of three years.

One of the surgical deaths which occurred 24 hours after surgery was that of a patient whose graft bled excessively after implantation. Although the bleeding was controlled, massive transfusions had been required, and the patient died without other explanation being found at autopsy.

Portions of the various bifurcations selected for suitable size were used in nine thoracic aneurysms, with two deaths. It is important to note that one of the fatalities was due to bleeding through the material.

Early in the present series of operations for aneurysm, performed since the previous report, occasional prostheses were encountered in which the weaving of the seam at the angle of the bifurcation had left a tiny defect large enough to produce persistent bleeding when such a graft was used. Usually the small orifice was closed with a Dacron patch without great difficulty. In one case bleeding became apparent several hours after surgery. The patient was returned to the operating room, and bleeding from the defect was controlled successfully.

Fatal bleeding occurred in one case of aortic bifurcation replacement and in the case of thoracic aorta replacement. Severe bleeding, finally controlled, was encountered in four other implantations. In some cases the hemorrhage accompanied generalized recurrence of bleeding in the surgical wound and planes of dissection which previously had been brought to a usual state of hemostasis. The graft in these instances appeared to become pale, as compared with the usual hue of the material when it is sufficiently impregnated with fibrin and blood deposited during the preclotting and after restoration of flow. The question arises as to whether there was a defect in the clotting mechanism, such as diminished fibrinogen or increased fibrinolysis. The need for appropriate studies has been recognized by us, but they have not yet been made. Protamine, human fibrinogen, and calcium were administered parenterally in these cases, without convincing evidence of their effectiveness. The local application of protamine and thrombin similarly was tried, but whether the bleeding stopped in the majority of these troublesome cases because of therapy of this type or for reasons independent of therapy is not known.

Changes in the weaving of the bifurcation portion of the grafts were then instituted to eliminate defects in the seams. At the same time, in order to improve the consistency and decrease the porosity of the graft, the thread count was increased.

Crimped Woven Tube.—The early results obtained from the use of the flat woven tube made it abundantly evident that the construction had to be improved. The continued patency of the initially successful bypasses indicated that the material itself did not deteriorate or appear to stimulate thrombosis. The previously reported series of 19 implants resulted in 7 patent grafts. These seven grafts are known to be patent at time of this report, representing a 26- to 31-month follow-up.

There seemed to be two deficiencies to account for the high initial failure rate in the flat tube. One of these was the fact that the inability of the tube to curve limited bypasses to the confines of the thigh. The second factor also involved difficulties in the handling of the prosthesis during anastomosis of the end-to-side type. The most convenient method of producing flexibility in the Dacron tube appeared to be crimping, as previously employed by Edwards et al.,[5] who used heat and chemical treatment to crimp the nylon tube.

Dacron fabric will set in pleats or folds when compressed into a desired shape and set on a heated mandril at temperatures below the melting point of Dacron. When cooled, the tube has a spring-like adherence to its new shape. This heat-setting does not affect the strength of the Dacron yarn and does not require the application of any chemical agent. Tubes of 50-in. length and of a variety of diameters are threaded on copper or stainless-steel rods having a diameter such that the tube fits snugly on the rod. The 50-in.-length tube is then

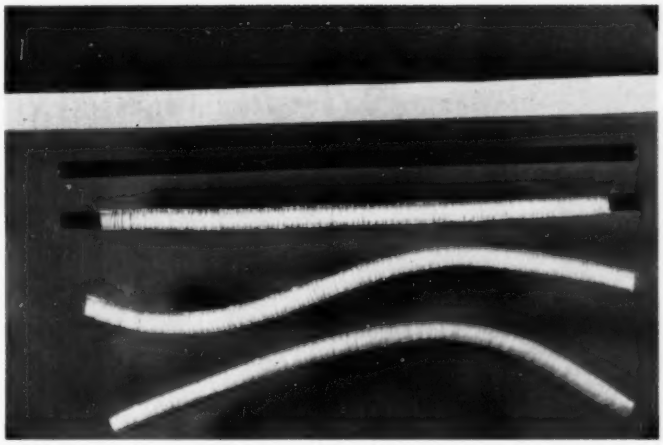
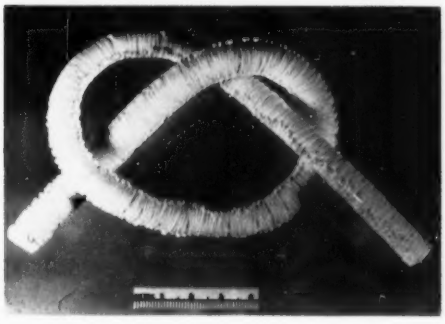


Fig. 1.—The process of producing the microcrimping is demonstrated. The flat Dacron taffeta tube, at the top, is threaded on the metal mandril, shown immediately below it. The fabric is compressed on the bar and heat-set. After it is removed, there is excellent flexibility, as shown. The lowermost graft was wrapped with tightly compressed Ivalon, in experiments aimed at elimination of preclotting.

crimped manually without external wrapping down to a 16- to 18-in. length. After heating and cooling, the finished tube is easily slipped off the mandril. It is then tightly crimped and has a spring-like flexibility (Fig. 1). It can be bent over acute angles of up to 120 degrees without kinking. The crimps in this tube are comparatively fine and may justify the descriptive term of "microcrimps," which we have applied to them (Fig. 2).

The crimped tube should be implanted under sufficient tension to restore about 75% of the original length. Under this tension it still retains an expansile capacity. This tension is comparable to that under which arterial homografts had been implanted for their best function. Also, the ability to curve without kinking is retained at this tension. If implanted without tension, the graft will buckle and angulate when subjected to arterial pressure and blood flow. Several grafts were implanted in this manner in dogs and retained excellent function, nevertheless, over a six-month period of observation (Fig. 3). The crimps, which are originally very small, become shallow when the tube is extended for implantation. This, together with the original thinness of the fabric, provides for a minimum of bulk of implanted foreign material.

Fig. 2.—The woven tube is sufficiently flexible to permit a marked angulation without loss of lumen, entirely as the result of the crimping.



The external selvage which appears at two points around the circumference of the tube has been found to be in no way detrimental to implantation or function. When the curves are made in the plane of the two flanges, the curving ability is actually increased rather than diminished. The presence of this longitudinal marker has helped in prevention of any twisting of the graft during implantation.

For end-to-side anastomoses of a bypass the beveled cut end may be lightly fused with a cautery at a temperature just below the visible heat. This results in an edge which, because of the tight weave of fine yarn, shows no tendency to fray, as contrasted with knits and braids. Heat fusion is not necessary, however, and recently we have simply used scissors to bevel or cut to proper length the crimped graft (Fig. 4).

Fig. 3A.—Arteriogram of a dog six months after implantation of a crimped tube into the aorta, as a bypass. The excessive angulation permitted intentionally at the time of insertion has not hampered the function.

Fig. 3B.—Another angulated graft inserted end-to-end into the canine aorta functioned perfectly over a six-month period.

Experimental Data.—In order to test the behavior of the crimped form of Dacron tube, a total of 46 thoracic and abdominal aortic end-to-end and bypass implantations were made in dogs (Table 2).

The initial observation was strikingly in contrast to the previous implantation of the noncrimped version of the prosthesis. Using the crimped tube, no instance of thrombosis or late failure of the graft has been observed up to a period of nine months. The complete freedom from early failure was considered evidence of ease of handling and a remarkable ability of the graft to accommodate for errors in placement or in judging length of the implantation. Several grafts of great excessive length were intentionally implanted and have demonstrated continued function (Fig. 5).

Fig. 4.—Simple beveling of the graft with scissors is adequate. The needle usually engages one or more of the microcrimps at the time of implantation, thus avoiding danger from fraying of the tightly woven fabric.

During the period of observation, and at the time the dogs were killed, aortograms were made in vivo. The graft was then explored, observed, and photographed, and microscopic sections were prepared. All 50 grafts of this group have remained patent during the period of observation. An accumulation of serosanguineous fluid was observed in a pocket surrounding eight implants (seven from the University of Illinois laboratory). Cultures were not obtained, and no explanation of this occurrence can be offered. The lining of the 3-month-old experimental grafts was uniformly smooth. The crimps were incompletely leveled; clots were absent (Fig. 6).

Aortograms disclosed an absence of significant kinking throughout the series. At three months most aortograms still showed

TABLE 2.—*Animal Testing Results* *
7-12 Cm. Tubes

	Univ. Illinois	Columbia P. & S.
Total implants	20	26
Plain crimp	14 (1 thrombosed)	20
Dacron plus Ivalon	--	6
Dacron plus silicone	6	4

46 grafts—1 thrombosed
Seromata or old hematoma—8 (all but 1 at Univ. of Illinois)

* Implants were 7-12 cm. tubes.

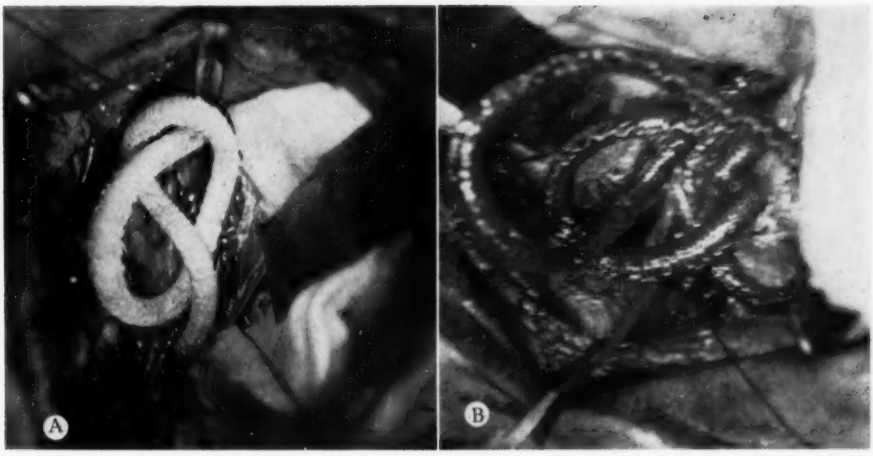


Fig. 5.—*A*, extremely long crimped tube has been implanted end-to-end into the abdominal aorta of a dog. *B*, the same graft is shown while functioning. There is blurring from pulsation of the prosthesis. *C*, arteriogram of this graft after several weeks reveals no recognizable thrombus in the lumen.

a crimp pattern at the edges of the contrast-medium-filled graft. The absence of tendency to kink was illustrated by one bypass graft placed in the aorta of the dog and left long enough to be tied in a large knot.

Results of Use of Microcrimped Prosthesis as Bypass.—After initial animal trials to explore the possibility of some unexpected adverse effect of crimping on the usefulness of the tube, this prosthesis was used in a series of clinical cases. There was an immediate and remarkable improvement in the results as compared with those obtained with the previous flat, noncrimped tube. Both the long available length of the prosthesis and its other characteristics, previously described, have contributed to the excellent results. The length was important in the sense that it provided unlimited ability to bypass the entirety of the disease process.

To date, 75 bypasses have been accomplished in 74 patients (Table 3). The most frequent bypass was from the common femoral artery level to the popliteal level. In all, 54 such restorative operations were done, utilizing an incision placed below the knee in 33 and an incision at or just above the knee in 21 for the approach to the popliteal artery. In one, a graft was placed in the superficial femoral artery to replace

Fig. 6.—*A*, arteriogram of crimped tube implanted under proper tension. There is a complete lumen at three months. *B*, this graft specimen confirms the conclusions drawn from the arteriogram.

TABLE 3.—*Microcrimped Femoral Tube*

	U. of Illinois		Columbia P. & S.	
	No.	Failures	No.	Failures
Aorta-popliteal	9	0		
Femoral-popliteal	40	5	14 *	2
Aorta-femoral	8	0	2 *	0
Aorta arch-carotid	1	0		
Aorta arch-subclavian	1	0		
Total 75 grafts, with 7 failures (9.3%)				

* With external coating of compressed Ivalon in two cases (successful).

a homograft which had become aneurysmal (Fig. 7). Of these 75 prostheses, 68 have maintained an entirely satisfactory blood flow during a nine-month period of observation. The reasons for the seven failures will be discussed later. Nine grafts were placed as bypasses from the abdominal aorta to the popliteal artery or from the common or external iliac artery to the popliteal artery. These nine operations have been successful. Ten bypasses were placed between the aorta and the common or superficial femoral artery, also without failure. Two grafts have been used to bypass occlusions of the carotid ‡ or subclavian arteries. One of these was between the aortic arch and the internal carotid artery. These two maintained a completely satisfactory flow for periods of three months and two months, respectively.

Because of the excessive blood loss noted occasionally through the fabric upon restoration of arterial flow in earlier cases, the first four crimped tubes used in New York had an external coat of highly compressed polyvinyl formalinized (Ivalon) sponge in addition. It had been observed in the laboratory that minimal blood loss occurred with these, even without preclotting. Clinically two grafts were used from the femoral to the popliteal artery and two from the common iliac to the common femoral artery, as bypasses. These have continued to function for almost a year. However, with the development of a higher count for the fabric, the porosity has been decreased

‡ Since the presentation of this paper, a crimped tube has been used successfully to replace a syphilitic aneurysm of the left common carotid artery.

Fig. 7.—A functioning crimped tube has replaced a homograft, which had become aneurysmal after one year. In this case, the end-to-end implantation yielded excellent peripheral pulses. Courtesy of Dr. F. F. McAllister.

sufficiently that there is only slight initial blood loss after preclotting.

As was noted above, 7 failures have occurred in the 75 grafts. Of these failures, two occurred in initially successful bypasses when, at the end of approximately a three-week period, each patient suffered rupture of the distal suture line at the popliteal level during some unusual activity. One of these patients fell as he entered his house upon discharge from the hospital. The second patient ruptured the distal anastomosis in turning his leg to get out of bed after discharge from the hospital. Two failures occurred a few hours after surgery. Both were instances in which the distal anastomosis had been done at the lowest possible level in the popliteal artery in the presence of severe disease, although pulses were immediately restored at the ankle and observed at the operating table. Both were thought to be instances in which the extent of disease in the popliteal artery at its bifurcation was responsible for thrombosis. In neither case could the anastomosis be retrieved at an immediate second operation, and one led to amputation of the extremity operated on. The fifth failure was in one of the bypasses from the common femoral artery down to the upper popliteal artery through an incision made on the medial aspect of the thigh above the knee. Thrombosis occurred four weeks after surgery. The patient was returned to the hospital and a second bypass implanted, the distal popliteal artery being approached through an incision distal to the knee on the medial aspect of the upper tibia. A stenosis of the popliteal artery distal to the first anastomosis was found, and the new anastomosis made to a very satisfactory segment of distal popliteal artery subsequently functioned in an entirely satisfactory manner.

Selection of Cases.—Previous criteria for the selection of cases have largely been abandoned in favor of direct surgical exploration of the popliteal artery bifurcation. This has been done as an initial step in patients scheduled for supracondylar amputation. In two patients included in this series, a patent popliteal bifurcation was found and a bypass was placed, with restoration of circulation and avoidance of loss of the limb.

Previously the clinical picture of good nutrition of the foot together with the arteriographic demonstration of a satisfactory distal arterial lumen was required. Four of our successful cases have been patients who had been denied surgery on the basis of an arteriogram prior to our present experience with this crimped graft.

The selection of the proximal site of anastomosis for the bypass received particular attention. In our previous experience using autogenous vein grafts, the limited length of graft obtainable from the saphenous vein of the patient made it necessary to place the proximal anastomosis within

the femoral triangle. In using the noncrimped Dacron tube, the inability of the tube to pass a joint made necessary the same proximal site. With the new construction there are adequate length and flexibility to permit the patient both hip and knee flexion. Consequently, there is a choice of proximal anastomosis sites, including the abdominal aorta and any point on the iliac artery. Evidences of partial occlusion proximal to the inguinal ligament is, therefore, carefully checked in patients having a femoral pulse. Such evidence includes an inequality of the femoral pulses and the presence of a bruit audible with the stethoscope over the femoral artery. When these signs are present, and in those cases having no femoral pulse, the proximal anastomosis is made within the abdomen at whatever point is necessary to gain an entirely unobstructed source of pulsatile flow.

Technique.—An incision is made longitudinally in the patient's artery at the point chosen for anastomosis, accurately matching in length one-half the circumference of the beveled cut end. A variety of methods of suture placement were employed by the various authors, without discernible differences in results. Stretching to restore three-quarters of the original length of the graft is actually an approximation, and it has become evident that there is wide latitude permissible in this part of the technique. An occasional graft has been left sufficiently long to be noticeably tortuous without affecting its good function.

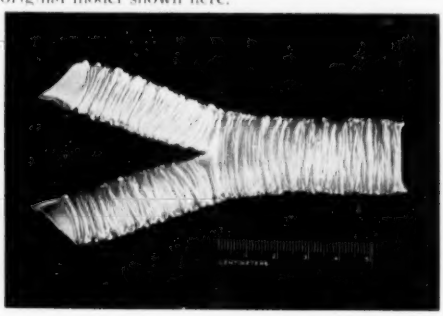
All bypass grafts have been placed beneath the deep fascia of the thigh, and beneath Poupart's ligament in cases in which the graft passes from abdomen to thigh. In passing from thigh to popliteal space, the graft lies within the adductor canal, enlarged to provide complete freedom of motion. Additional incisions are made to facilitate the accurate placement of the graft.

Mild systemic heparinization often was employed by the surgeons of the University of Illinois group. Observations made on the behavior of blood drawn for preclotting the graft were the empiric basis for giving heparin intravenously, in addition to injection of heparin into the distal artery during the period of obstruction. When the blood in the vessel in which the graft is preclotted coagulated in a period of less than two minutes and formed a firm, tenacious clot, 10 to 20 mg. of heparin was given intravenously before the anastomoses were begun. In following this regimen, one patient was overheparinized, and subsequent bleeding through the graft ceased within a minute or two of neutralization of heparin by protamine.

Preclotting of the grafts has been routine. Therefore, no observations were made as to the rapidity with which bleeding would stop if a nontreated tube were to be implanted. The preclotted graft is allowed to stand exposed to air for a period of more than 10 minutes before it is passed through the tunnel in the patient's extremity, where it comes into contact with fat. With preclotting the amount of bleeding through the graft when circulation is restored is subject to tremendous variation. Most grafts bleed momentarily when the distal clamps are removed. In a few, intermittent occlusion of the artery above the proximal anastomosis is even required. On the other hand, some grafts are entirely dry. No instance of dangerous bleeding through graft occurred in peripheral bypasses.

Crimped Woven Bifurcation.—Since March, 1958, the bifurcations have been

Fig. 8.—Woven bifurcation with microcrimping. Several sizes are available, and the length of the iliac arms has been increased further, since the original model shown here.



subjected to crimping in the same manner, which has added materially to the flexibility and adaptability of the prosthesis (Fig. 8). Approximately a dozen implantations have been performed during the past three months, both as end-to-end replacements and end-to-side bypasses for aneurysm or occlusive disease. To date all have been successful.

Comment

During the early years of the past decade, the homograft played a vital role in the renaissance of vascular surgery. Various methods of preservation were developed to permit greater convenience and broader application, as well as prolonged storage time. Many experimental studies were reported, but few contained long-term observations. In one, Coleman and Deterling [1] described the increase in calcification, destruction of elastic fibers, and gross thinning of aortic homografts during periods of 18 months to 4½ years in the abdominal aorta of dogs. Creech et al.[2] and Gentsch et al.[6] demonstrated the susceptibility of preserved homografts to degeneration in excess of that shown by normal aorta in dogs subjected to stress conditions. Although Creech et al.[7] did not find alarming degeneration in aortic homografts recovered after one to two and a half years in four human cases, Szilagyi,[8] Humphries,[9] Deterling,[10] and others have observed aneurysmal degeneration of homografts used in patients with peripheral occlusive vascular disease.

Since the demonstration in 1952 by Voorhees et al.[3] that synthetic-fabric prosthesis could function satisfactorily in the arterial system, there has been an increasing interest in synthetic replacements. After a period of trial and error, several types of commercially available synthetic replacements have emerged. As anticipated in an earlier study evaluating synthetic materials,[11] both Dacron and Teflon appear to be the most satisfactory for use under stress in mammalian tissues. The virtues of Teflon have been well described by LeVeen and Barberio,[12] Girvin et al.,[13] Harrison,[14] Szilagyi,[15] Edwards and Lyons,[16] and others. It is of interest that Edwards now prefers a crimped knitted prosthesis of Teflon to his original braided nylon graft.[5]

Experience during the past few years has yielded valuable information regarding the factors important in the construction of a synthetic prosthesis. In the past, excellent function has been achieved by braided, knitted, and woven prostheses. The convenience afforded by simple cutting of the ends without fear of unraveling has placed the current fine-denier, tightly knitted, or woven crimped types in a more favorable light, however.

Although the presence of seams was thought by Whittlesey et al. to incite thrombosis, experiments in our laboratory with fabric prostheses with as many as six seams have failed to confirm this belief. The selvage edge or external seam of the prosthesis being reported has been helpful as a marker to avoid torsion of the graft. When the graft is distended, the internal seam is not apparent.

Porosity has been discussed vigorously, with no conclusions yet reached regarding the optimal degree. The trend has been to decrease porosity by increasing the thread count and decreasing the twist of yarn. Nevertheless, it is still necessary to preclot the synthetic prostheses in order to minimize blood loss when flow is reestablished. In our experience, more blood loss occurs with Teflon replacements despite preclotting, since yarn of this material cannot be woven or knitted as tightly as can that of other materials. The present tight weave of our replacement permits only very transient weeping of blood, in contrast to the earlier one.

The flexibility achieved by Edwards and Tapp by crimping [5] has been subsequently employed by De Bakey [17] in a knitted Dacron prosthesis and by us in the woven Dacron replacement described in this report. Functional results have been superior to those obtained with noncrimped tubes. Flexibility has also been obtained through the use of Helanca yarn in noncrimped

tubes of nylon or Teflon, as described by Szilagyi et al.[15] and Whittlesey et al.[18]

The thickness of the wall of the replacement has some practical aspects; whereas a heavy braid or knit may be very satisfactory for use in the aorta, it is less desirable for use in the extremities or neck. Furthermore, with minimal torsion, a thick-walled prosthesis will buckle despite crimping. Our graft can be twisted through 180 degrees in 9 in. of length without loss of lumen.

Although further modifications can be expected as greater experience is obtained with synthetic replacements, the one described in this paper has proved to be very satisfactory. Efforts aimed at the elimination of the need for preclotting are continuing. To date, external additives, such as silicones, Ivalon, Curon,§ and collagen gel ‖ have not been entirely satisfactory. Additional work is needed in establishing proper standard sizes and lengths of prostheses for use in any case. Development of multibranched grafts is being considered, although side-arms can be sewn into most of the current commercial prostheses. The great strides in prosthetic construction during the past year would seem to make the continued use of homografts almost unwarranted at the present time.

The recent experimental studies performed at Columbia University College of Physicians and Surgeons by Dr. Yousif Al-Naaman were of valuable help.

25 E. Washington St. (Dr. Julian).

§ Supplied by Mr. Garth.

‖ Prepared by courtesy of Davis & Geck, Danbury, Conn.

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Effects of Infection and Exposure on Synthetic Arterial Prostheses

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The development of synthetic vascular prostheses has greatly extended the indications for and employment of procedures for replacement or bypass of occluded arterial segments. Problems which limit the usefulness of homografts, namely, availability and difficulties of sterilization and preservation, are obviated by the use of synthetic grafts to the extent that the artificial materials have almost supplanted the naturally occurring homograft as blood vessel substitutes.

As experience with synthetic grafts accumulates, it becomes apparent that they possess certain distinctive properties. Among these is their ability to function as vascular channels when uncovered by surrounding soft tissues and/or in the presence of infection. This quality, not possessed by homografts, would appear to be fortunate indeed, and so it is. Yet it is not an unmixed blessing! For while an exposed or infected synthetic prosthesis continues to function as a blood conduit, it also functions as a foreign body, vigorously resisting attempts to cover it and to eradicate the infection. Obviously, these circumstances create serious problems. This report is concerned with six cases in which synthetic vascular replacements were employed and in which exposure and infection were complicating features.

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Report of Cases

CASE 1.—A 52-year-old man was admitted to Charity Hospital on March 13, 1957, with a history of intermittent claudication in both calves and an ulcer on the left fifth toe. Femoral arteriograms revealed segmental occlusion of both superficial femoral arteries. On March 22, a bypass graft of crimped nylon was anastomosed to the common femoral artery, above, and to the popliteal artery, below, on the left. Although the foot became warmer after operation, no pedal pulses were present. On March 29 the lower portion of the wound appeared to be infected and was opened and packed with iodoform gauze. Culture revealed an enterococcus sensitive to erythromycin, and Staphylococcus aureus, which was sensitive to chloramphenicol U. S. P. (Chloromycetin), novobiocin, and oleandomycin. Treatment with erythromycin and chloramphenicol was instituted, and on April 11 the patient was operated upon with the intention of removing the graft. However, an

Fig. 1 (Case 1).—Arteriogram of the exposed femoral prosthesis made at the time of drainage of the infected wound.

arteriogram disclosed that the graft was functioning satisfactorily; therefore, the entire bed of the graft was opened and packed with iodoform gauze (Fig. 1). The wound was dressed daily and healed rapidly except at each end, where segments of the graft, 6 or 7 cm. in length, protruded (Fig. 2). On May 5 a skin flap was elevated on the lateral aspect of the thigh and the redundant loops of graft placed beneath it. However, the graft again extruded itself from the wound. On June 7, the entire wound was reopened, the graft was buried behind the full length of the sartorius muscle, and the wound was carefully closed in layers, with multiple drains left along the course of the incision. Subsequently, it became apparent that the wound was still infected, and the graft was removed, although still functioning. Gangrene developed in the foot and eventually required amputation at the hip. The patient was finally discharged on Oct. 15.

Comment.—In this patient an arterial graft became exposed as a result of wound infection. This responded well to incision through the entire bed of the prosthesis, although, once uncovered, the graft was excessively long and formed loops near each end, which projected above the surface of the wound. Thus the wound healed rapidly, leaving these loops exposed. The prosthesis functioned satisfactorily for about four months, but attempts to cover the graft were unsuccessful because of persistent infection and excessive length. These factors eventually led to removal of the prosthesis and amputation.

Case 2.—A 17-year-old youth sustained a shotgun wound of the right thigh at close range on June 12, 1957. There was extensive loss of skin, subcutaneous tissue, and muscle, and the contents

Fig. 2 (Case 1).—After initial drainage the wound has healed, but two redundant loops of the graft are exposed.

Fig. 3 (Case 2).—Eight weeks after implantation the graft lies exposed in a bed of granulation tissue.

of the femoral sheath, including the artery, vein, and nerve, were destroyed. He was admitted to the Lallie Kemp Charity Hospital, Independence, La., a few minutes after injury with the blood pressure and pulse unobtainable. Massive administration of whole blood was begun. Three hours after admission his blood pressure had been adequately stabilized and operation was performed. Extensive debridement was carried out, and continuity of the femoral artery was restored by means of a crimped nylon tube anastomosed end-to-end with the severed femoral artery. A transverse fracture of the femur was identified at this operation. Because of the extensive muscle loss, the adductor muscle was severed from its origin and sutured over the graft. The remainder of the wound was packed open because there was extensive oozing from the traumatized muscle. The following day bilateral fasciotomies were performed on the right leg, and the patient was transferred to Touro Infirmary. Thereafter, he was anuric for 21 days. During this time it was necessary to perform dialysis with the artificial kidney on three occasions. During the third week of anuria further necrosis of muscle appeared in the thigh, as well as in the muscles on the anterolateral aspect of the leg. Debridement of this necrotic muscle exposed the graft in the thigh. He received only local antibiotics and frequent changes of dressing. By July 20 urinary output was adequate. Cultures of the wound consistently showed Pseudomonas aeruginosa organisms, which were sensitive only to neomycin. The wound of the thigh was dressed daily with dry gauze and irrigated with 1% neomycin solution. On this regimen the wound contracted rapidly, and approximately two-thirds of the exposed portion of the graft was covered by healthy granulation tissue (Fig. 3). On Aug. 20 a large flap of skin and subcutaneous tissue was elevated from the lateral aspect of the thigh and transferred medially to close completely the remaining wound. Fasci-

otomy wounds in the leg were completely closed at the same time. Five days later there was purulent drainage from beneath the skin flap. On Sept. 15 it was necessary to open a portion of the medial suture line because of persistent drainage from beneath the skin graft, and after this a small segment of the graft reappeared in the base of this wound (Fig. 4). Daily dressings were again performed in the hope that the remaining open portion of the wound would close spontaneously. By this time the femoral fracture had healed in satisfactory position (Fig. 5). On Oct. 6, the patient became febrile, and for the first time cultures from the wound revealed a Staphylococcus. Six days later bleeding occurred from the base of the wound. Only a small part of the wound of the thigh was open and a 1 in. segment of the nylon tube was exposed in the base of this residual wound. Although it was functioning, the arterial graft was removed because the patient was febrile and no other source of infection could be found. The extremity remained viable. The wound of the thigh was dressed and permitted to remain open. On Nov. 13 an abscess on the dorsum of the foot was identified and drained. Culture of the material in this abscess revealed S. aureus. The wound of the thigh healed rapidly after removal of the graft. Roentgenograms of the foot disclosed that the abscess on the dorsum involved the fifth metatarsal. Upon adequate drainage this infection was controlled, and the patient was discharged on Dec. 20, 1957.

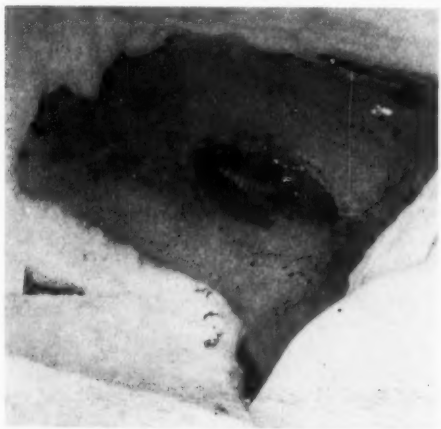


Fig. 4 (Case 2).—Appearance of the wound at four months. A pedicled flap failed to cover the graft, owing to persistence of infection.

Comment.—Here, a nylon graft was used as an arterial replacement in an area of extensive soft-tissue loss. The remaining parts were inadequate to cover the prosthesis, and, as a result of poor healing secondary to severe uremia, these tissues sloughed, leaving the graft completely exposed. Nevertheless, in this condition it functioned satisfactorily for three months. Attempts to cover it were unsuccessful because of infection. Furthermore, formation of septic emboli occurred, resulting in osteomyelitis of the metatarsals. When the graft was removed, the limb remained viable, and the wound healed promptly.

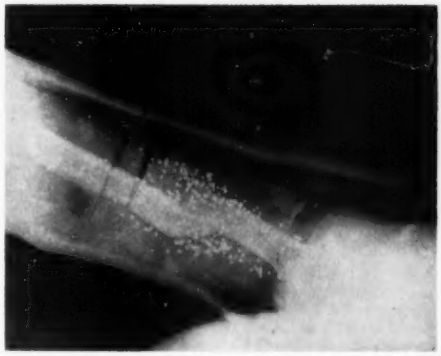


Fig. 5 (Case 2).—The femoral fracture healed satisfactorily within 12 weeks.

Case 3.—A 61-year-old man first noticed symptoms of arterial insufficiency in 1956. Examination at the time of admission, in January, 1957, revealed absence of pulses in the left lower extremity. An aortogram disclosed stenosis of the left common iliac artery, with partial aortic occlusion as well. In January, 1957, the aortic bifurcation was resected, both iliac arteries were closed, and a bifurcation nylon graft was anastomosed end-to-end with the proximal aorta and end-to-side with the common femoral arteries bilaterally. He was discharged from the hospital 14 days after operation, with pronounced improvement in his symptoms. In October a pulsating mass appeared in the left groin. He was readmitted to the hospital on Oct. 24 because of the sudden appearance of anesthesia and loss of mobility of his left lower extremity. At operation a large, false aneurysm of the common femoral artery was found, arising as a result of disruption of the anastomosis between nylon graft and femoral artery (Fig. 6). About 5 cm. of the distal end of the graft was resected, together with the anastomotic site in the common femoral artery, and a piece of $\frac{5}{16}$ in. nylon tubing was anastomosed end-to-end to the original graft proximally and to the superficial femoral artery distally (Fig. 6). At completion of operation there

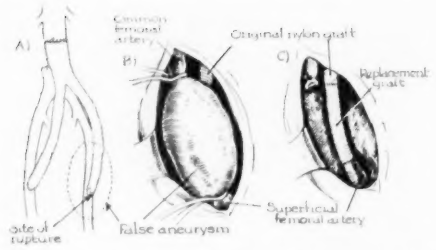


Fig. 6 (Case 4).—Diagrammatic representation of false aneurysm following bypass procedure for aortoiliac occlusion (*A* and *B*). The final appearance, after excision of the aneurysm and the leaking anastomosis, followed by end-to-end reconstruction of arterial continuity, is shown in *C*.

was excellent pulsation of the graft and the arteries of the left foot. On Nov. 11 it became apparent that the wound was infected; therefore, it was opened widely to reveal the graft pulsating in the base of the wound. Cultures of the wound at this time revealed S. aureus, Proteus morganii, and enterococci. On Nov. 28 there was sudden onset of bleeding from the wound. At operation the graft was ligated proximally through a small incision in the left groin and divided. The wound in the inguinal region was closed, and the femoral artery was then ligated distally in the open wound of the upper thigh. The nylon tube was removed through the wound in the thigh. It was observed that the femoral artery had a soft, somewhat mushy, consistency, and separated readily from the prosthesis. Culture of the ligated end of the graft yielded S. aureus. On Dec. 6 a circular amputation through the left thigh was performed. The wound healed rapidly except for a residual sinus in the left groin.

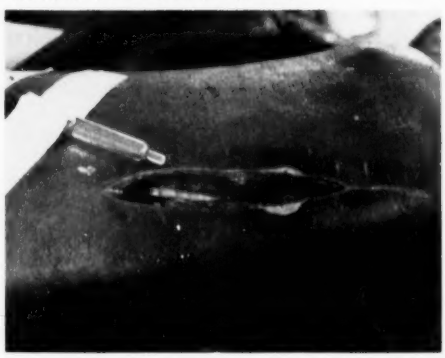
Comment.—A false aneurysm appeared around one limb of a bifurcation graft 10 months after its insertion. There was no conclusive evidence that infection played a part in this graft failure. Nonetheless, surgical correction of the aneurysm was followed by obvious wound infection, exposure of the graft, and bleeding. Removal of the graft on the involved side only led to amputation of the extremity. Seven months later there is a small sinus at the ligated end of the graft. He has no evidence of infection about the portion of the graft supplying the remaining lower extremity.

Case 4.—A 53-year-old man was admitted on June 28, 1957, with a history of intermittent claudication in the left leg for three months. An arteriogram demonstrated segmental occlusion of the femoral artery at the lower end of the adductor canal. On July 18 the obstructed area was bypassed with a crimped nylon tube. Anastomoses were made to the common femoral artery, above, and to the popliteal artery, below. The course after operation was satisfactory, and he was discharged on July 27. During the ensuing few months he was followed in the outpatient clinic, where examination disclosed excellent function of the graft, and he returned to work. On Nov. 28 he was readmitted to the hospital with a large abscess in the popliteal fossa, which required drainage. The graft, exposed at the base of the abscess cavity, continued to function (Fig. 7). The wound was packed, and penicillin and streptomycin were administered. After several days the wound was irrigated continuously for 24 hours with a solution containing penicillin, neomycin, and bacitracin. At the end of this time secondary closure was performed without drainage, using interrupted stainless-steel wire sutures. Treatment with antibiotics was continued for 15 days, and 26 days after secondary closure the patient was discharged. Examination seven months later revealed excellent pedal pulses and no evidence of infection.

Comment.—Infection of the nylon graft did not become apparent until four months after operation in this instance. Despite staphylococcic infection and exposure at its distal anastomosis, the graft continued to function. Local and systemic antibiotic therapy permitted successful secondary closure of the wound.

Case 5.—A 58-year-old man was admitted to the Touro Infirmary on Feb. 17, 1957, with symptoms of occlusion of the right femoral artery. On examination there were no pulses palpable below the femoral artery on the right. An arteriogram on

Fig. 7 (Case 5).—Photograph of open wound after drainage of the abscess. The prosthesis is visible in the base of the wound.



Feb. 18 revealed segmental occlusion of the lower femoral artery. A bypass operation was performed on Feb. 25, using a crimped nylon tube. The patient recovered satisfactorily and went home in 10 days. On March 20 he was readmitted to the hospital, complaining of pain in the lower incision and a temperature of 100 F daily. Examination revealed a hematoma about the graft beneath the distal incision. At operation there was active bleeding from the anastomotic site. The popliteal artery was ligated and the graft removed except for about 2 cm. at the proximal anastomosis. This was left because the femoral artery at this level was patent. A right lumbar sympathectomy was also performed. Culture of the wound revealed S. aureus, which was sensitive to tetracycline U. S. P., streptomycin, and chloramphenicol. An April 23, a pulsating hematoma of the right thigh beneath the upper incision was evident. This was incised and the remaining portion of the nylon tube removed. This necessitated ligation of the superficial femoral artery. At this time an abscess on the dorsum of the foot became apparent and was incised and drained. S. aureus was cultured from this wound with the same sensitivity to antibiotics as the organism which was cultured from the lower wound on March 20. Roentgenograms of the foot disclosed destruction of the fifth metatarsal, indicating that the abscess on the dorsum of the foot was secondary to hematogenous osteomyelitis. This lesion has subsequently healed.

Comment.—In this case infection in the thigh could not be controlled until all of the offending foreign body was removed. The most significant feature of this case was the development of septic emboli to the foot.

Case 6.—A 67-year-old white man was admitted to Charity Hospital on March 7, 1957, with complete obstruction of the left external iliac artery, confirmed by arteriography. On March 28, an iliofemoral bypass was performed on the left, using a crimped nylon tube. The wound in the upper thigh became infected; the prosthesis ceased to function, and the left lower extremity became gangrenous. On May 22, a circular amputation through the upper portion of the left thigh was carried out, and the distal portion of the graft was removed. Cultures of the wound revealed S. aureus. The amputation site failed to heal, and a draining sinus in the upper thigh at the site of the nylon tube persisted. The remaining portion of the infected graft was removed on July 29, but it was necessary to ligate the left common iliac artery. Progressive gangrene of the thigh, buttock, and pubic area developed, and the patient died on Dec. 5, 1957.

Comment.—Following cessation of function of a synthetic graft, infection became evident. Inability to eradicate the infection necessitated removal of the prosthesis and interruption of a functioning iliac artery. This led to gangrene of the left hindquarter and the death of the patient.

General Comment

Although these cases comprise a somewhat heterogeneous group, they have several important features in common; that is, crimped nylon tubes were employed as arterial prostheses in each, and five of the six patients had a functioning graft which was exposed in an infected wound for varying periods of time.

In three patients serious bleeding occurred on one or more occasions, and in every instance arose from an anastomotic site. Bleeding through the wall of the graft did not occur. The gross appearance was the same in all cases. The host artery was edematous and friable, and sutures had pulled out of it at one or more points. In one of these patients (Case 2) the anastomotic site from which bleeding occurred was at a distance from the original area of infection. Three months elapsed before bleeding occurred. In the other two patients the anastomotic site which bled was involved in the original infection. In both these patients bleeding appeared within a few days of the onset of the infection. This suggests that the necessity for prompt action to prevent bleeding will depend on whether an anastomotic site is involved in the infection.

Microscopic examination of a nylon graft removed after it had functioned in an open wound for three months revealed a mature connective tissue lining with only slight infiltration of inflammatory cells. At one point, however, there was a microscopic abscess within this lining membrane (Fig. 8). This patient, and one other of this series, developed abscesses in the metatarsals which were a result of septic emboli originating in abscesses adjacent to the

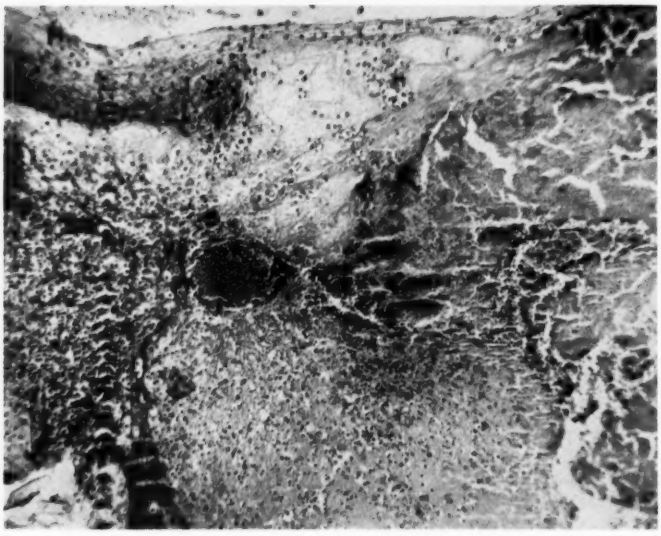


Fig. 8. — Photomicrograph demonstrating an abscess in the lining of the prosthesis removed in Case 2. This patient developed a metastatic abscess in his foot.

lumen of the vessel. In another graft, removed in Case 5, excessive thickness of the lining membrane was found (Fig. 9). This change has been recognized in prostheses placed in infected areas in experimental animals.

The infecting organisms in each of these cases was the hemolytic S. aureus, and in each instance the organisms were sensitive to one or more antibiotics. All organisms showed in vitro resistance to penicillin, but most of them were sensitive to neomycin, chloramphenicol, or erythromycin. In addition to the Staphylococcus, Pseudomonas, enterococci, and Escherichia coli were cultured from several of the wounds. In four instances the Staphylococcus appeared to be an invasive agent, producing systemic and local evidence of severe infection and necessitating removal of the graft. On the other hand, in two patients the wound healed without removal of the arterial graft, even though the Staphylococcus was repeatedly cultured from the wounds. In

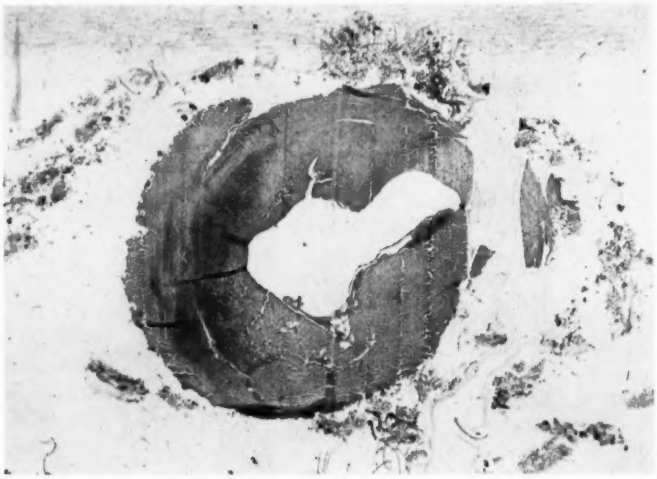


Fig. 9.—Photograph of a cross section of the prosthesis removed in Case 5, demonstrating the greatly thickened fibrin lining.

all these cases nylon grafts were used. Experimental studies[5-7] and available clinical reports[8-10] suggest that the retention of any foreign body in the presence of infection is dependent upon its reactivity in the tissues of the host. Nylon is more of an irritant in tissues than Orlon, Dacron, or Teflon,[5] and it may be that the conclusions reported here can be modified on the basis of further experience with less reactive materials.

On the basis of this experience some conclusions are probably warranted. Contrary to earlier impressions that the use of synthetic prostheses is contraindicated in arterial trauma, they would appear to be the agents of choice under certain circumstances. Where adequate soft tissue is available after thorough debridement and a gap in arterial continuity exists, a synthetic prosthesis offers significant advantages over both homografts and venous autografts as regards continued patency and survival as a functioning unit.[2] Should infection occur, the patient would be safer from both hemorrhage and thrombosis with a synthetic prosthesis than with a homograft or venous autograft. The indications for use of a synthetic graft are even more definite when arterial loss is combined with extensive soft-tissue destruction, making wound closure impossible, or where there is extensive dead space, or where the wound cannot be closed primarily because of excessive oozing from traumatized large muscle masses. In these situations a synthetic prosthesis can be placed in the defect and left exposed with little risk of hemorrhage or thrombosis, provided the anastomoses are adequately covered.

In two cases of this series (Cases 3 and 4) dilatory management of hematomas probably contributed to the development of serious infections. The appearance of a hematoma in the wound or in the retroperitoneal space following insertion of a synthetic prosthesis requires active treatment. In some instances the hematoma communicates with the arterial lumen through a leaking anastomosis. Temporizing with this situation can lead to devitalization of the overlying skin and wound edges, as well as to changes in the artery. Even if the hematoma does not communicate with the arterial lumen, it interferes with the adaptive responses of the patient to the arterial substitute and provides an ideal culture medium for bacteria. An aggressive attitude in the management of hematomas will prevent infections. Thus, where a hematoma is known to be present, the patient should be reoperated upon promptly. The entire wound should be opened and the hematoma completely evacuated. If an arterial leak exists, this must be repaired. Then the wound should be irrigated with a solution of 1% neomycin and bacitracin (500 units per cubic centimeter) and closed without drainage with stainless-steel wire sutures through all layers.

When there is an established infection with abscess formation, the problem is more formidable.[3,4] As demonstrated by the cases reported here, infection of a synthetic graft may not become evident for months after operation. This complication may be masked by the prophylactic administration of antibiotics or, in the case of aortic replacement, by the natural concealment of the area involved. Generally, patients in whom infection exists do not recover normally from operation, and the period of convalescence is prolonged. Usually a slight elevation of temperature persists after discharge from the hospital. Admittedly, these manifestations are inconclusive and, under other circumstances, not sufficient cause for alarm. However, experience indicates that these symptoms portend the appearance of frank abscess formation, severe hemorrhage, and even death of the patient. It appears, therefore, that decisive surgical intervention is indicated in management of the infected synthetic graft.

The proper approach to this problem depends upon the location of the graft and whether or not an anastomotic site is immediately involved. Thus, should a syn-

thetic prosthesis employed for femoral bypass become infected without involvement of an anastomosis, treatment should consist of opening the wound widely so as to expose completely the infected portion of the graft. Continuous irrigation of the wound with a solution of neomycin and bacitracin for 24 hours, followed by closure of the wound without drainage, should be effective in most instances.

It has been observed that crimped nylon prostheses gradually elongate as a result of flattening of the pleats. In some instances in the present series this led to the formation of redundancy of the prosthesis in the open wound, which prevented obliteration of dead space at the time of secondary closure. It is suggested that a portion of the graft be resected if necessary to cause the prosthesis to lie at the base of a wound.

The early recognition and treatment of infection are particularly important, for, although in the initial stages the infections process may involve nonanastomotic areas, eventually, if allowed to persist, infection will extend to the anastomoses. Infection of anastomotic areas is almost invariably accompanied by disruption of the suture line and hemorrhage. In the case of femoral-artery replacements false aneurysms form about the sites of disruption and are evident grossly. In the case of infection involving an aortic prosthesis, the absence of tissue planes and retaining structures results in extensive loss of blood and manifestations of hemorrhagic shock. In some instances disruption has occurred not at the anastomoses but in areas on the aortic wall to which occluding clamps were applied at operation.

Management of infection involving an anastomosis of a synthetic prosthesis to an artery is difficult indeed. Repair of the disrupted suture line is impossible, and removal of the graft with repair of the sites of anastomosis, thereby providing an adequate arterial lumen, may also be impossible. Thus, one must either remove the graft and ligate the involved arteries or remove the infected graft and attempt to bypass the infected area with another prosthesis placed in a sterile field. The former procedure is often followed by serious ischemia of the part, since sacrifice of the artery to which the prosthesis is joined also involves sacrifice of important collaterals. Bypass in a sterile area is extremely difficult and in some situations impossible to execute. In general, infections of synthetic grafts in the extremities with breakdown of the anastomoses should be treated by removal of the graft and ligation of the vessels involved. Sympathectomy may be performed at the same time. If circumstances permit, a new bypass should be attempted. In instances where abdominal or thoracic aortic grafts are involved and ligation would be fatal, bypass from a higher level should always be attempted. Complete drainage of the infected area and the local use of neomycin and bacitracin should also be carried out.

Infection of a femoral or iliac limb of an aortic bifurcation graft creates a peculiar problem, since it is essential that the infection remain confined to the involved branch. Under these circumstances the graft should be approached proximal to the infected area and the limb of the prosthesis divided, permitting removal of its involved portion through the infected wound. This may involve sacrifice of the major artery to a lower extremity, but this is justified if the aortic and opposite iliac portions of the graft remain free of infection and continue to function. In these circumstances sacrifice of a limb may be the only alternative to loss of life.

Summary

Synthetic arterial prostheses have been observed to retain their function as vascular channels even in the presence of infection or when uncovered by soft tissue. In such circumstances, however, they also act as foreign bodies, hindering control of the infection and resisting attempts to cover them. Six cases of infection of synthetic grafts were treated. A functioning graft has been retained in two of these patients. In four

patients the graft had to be removed. Hemolytic S. aureus was the infecting organism in each case. All organisms were sensitive to several antibiotics. Bleeding occurred only from exposed anastomoses. Aggressive treatment of hematomas is an important factor in prevention of these infections. The ability of synthetic grafts to function in the presence of infection enhances their usefulness in arterial restoration after trauma. Adequate treatment of established infections around arterial grafts involves wide external drainage of the infection, followed by intensive local and systemic antibiotic therapy. Secondary closure of the wound may then be attempted. Should infection persist, the graft must be removed. This will often entail sacrifice of a functional artery and should usually be combined with sympathectomy or, if possible, construction of a new arterial channel in a sterile field.

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DISCUSSION

DR. JOSEPHUS C. LUKE, Montreal: I should like to report four of these very serious mishaps, three in homografts and one in a synthetic graft, and bring out a point which might minimize this tragic complication. All these cases were of femoropopliteal grafts and occurred in fat people. Two occurred at late intervals after operation, one being five and the second seven weeks later, and the patients had been discharged from hospital some weeks previously. Two others occurred three weeks before being discharged. Three had induration and a mild degree of inguinal wound infection without breakdown of the wound, and the fourth had a more acute groin wound infection, necessitating opening and draining of the wound. All grafts were functioning at the time of their dehiscence.

In the two in which we reoperated, the anastomotic sutures had pulled out of the prosthesis in the homograft case, but in the synthetic graft they had pulled out of the host vessel. Three out of the four graft disruptions resulted in thigh amputations.

I would suggest good preoperative bathing in all these cases, especially the fat patient. The skin should be prepared on several occasions with hexachlorophene soap, as in an orthopedic operation.

DR. ROBERT J. SCHRAMEL, New Orleans: I have nothing to add other than to say that there are a number of other points in prevention and in treatment of these complications that we did not go into at this time, but which will be found in the text of our paper.

Evaluation of Thromboendarterectomy in Treatment of Obliterative Arterial Disease

NORMAN E. FREEMAN, M.D., and GERALD J. NICHOLSON, M.D., San Francisco

Direct surgery on arteries in the treatment of obliterative arterial disease has been used extensively since the pioneering work of Dos Santos, published in 1947.[1,3,6,9,14] Thromboendarterectomy was followed by the use of arterial homografts[2,10,13] and subsequently by the use of plastic prostheses, either as replacements or as bypasses for the involved segments. We have employed thromboendarterectomy almost exclusively over the past seven years. The present paper deals with a critical evaluation of this procedure based on experience in 87 cases treated on the private service of one of us (N. E. F.).

For the purpose of analysis, these cases have been divided into two main groups, depending upon whether the operation was performed for the relief of intermittent claudication or for the severer form of the disease, when the presenting complaint was rest pain, ulceration, or gangrene. As our experience has developed, we have been forced to become more selective, reserving operation for claudication only in those cases in which the patient was incapacitated by his inability to walk; in the ischemic cases, operation was reserved for those in which conservative methods of treatment had failed and in which amputation otherwise appeared to be inevitable.

As with any new therapeutic procedure, the complications and mortality were expectedly higher in the earlier cases; but all patients operated upon between December, 1950, through January, 1958, have been included.

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Results

A. Claudication.—Of the 49 patients having 50 operations for intermittent claudication, 42 were men, with a mean age of 54.9 years. The age of the seven women was slightly greater, 58.4 years. The data on these cases are contained in Table 1. The majority of these patients were suffering from the Leriche syndrome, with occlusive disease limited to the aorta and iliac arteries, whereas the more distal arterial system was relatively unaffected. Follow-up studies showed that the arterial system remained patent in 76% of the cases, even up to six years after operation (Table 2). There were two operative failures and four postoperative deaths in this group. Recurrence of thrombosis or occlusion of the proximal or distal arteries, due to advance of the obliterative disease, occurred in subsequent years in seven cases, or 14% of the cases. When the femoral or popliteal arteries were involved, the only patient whose artery has stayed patent for more than three years has been on continuous anticoagulant therapy.

Recurrence of thrombosis did not necessitate amputation in any of the patients. The spontaneous development of collateral circulation has resulted in relief of symptoms in two patients, and in an additional five patients the disability is only moderate.

Two patients died some months after operation of rupture of an aneurysm at the site of thromboendarterectomy. In both these cases infection was present and probably contributed to the fatal dissolution.

TABLE 1.—*Claudication* *

Case No.	Sex	Age	Date of Surgery	Operation	Result	Follow-Up
1	M	61	12/13/56	Common femoral	Well	14 mo.
2	M	47	1/17/57	Aortoiliac	Well	10 mo.
3	F	59	4/5/55	Aortoiliac	Well	32 mo.
4	M	48	9/8/53	Aortoiliac	Well	36 mo.
5	M	45	6/17/52	Aorta	Failed	Died, coronary occlusion, 39 mo.
6	M	47	4/5/56	Aortoiliac renal	Well	26 mo.
7	M	60	12/6/56	Aortoiliofemoral	Well	11 mo.
8	M	51	7/3/52	Aortoiliac	Well	46 mo.
9	M	68	10/31/56	Aortoiliofemoral	Well	18 mo.
10	M	61	10/6/55	Aortoiliac	Well	30 mo.
11	F	55	3/22/56	Aortoiliac	Partial recurrence at 25 mo.	25 mo.
12	M	45	9/10/53	Aorta and left iliac	Well	52 mo.
13	M	58	9/16/57	Aortoiliac	Partial recurrence at 2-3 mo.	11 mo.
14	M	56	2/10/55	Aortoiliac	Well	36 mo; died 39 mo., acute infectious hepatitis
15	M	46	7/7/55	Aortoiliac	Well	27 mo.
16	M	61	5/24/55	Aortoiliac	Well	33 mo.
17	F	54	9/11/52	Aortoiliac	Partial recurrence	64 mo.
18	M	49	9/21/54	Aortoiliac	Died, ruptured aneurysm	6 mo.
19	M	72	3/20/53	Right extrenal iliac	Well (as to legs)	53 mo.
20	M	57	12/10/57	Aortoiliac	Well	5 mo.
21	M	62	2/8/52	Aortoiliac	Well	65 mo.
22	M	64	2/6/57	Aortoiliac	Well	8 mo.
23	M	45	5/16/55	Femoral	Recurrence after 12 mo.	23 mo.
24	M	57	11/10/55	Aortoiliac	Well	27 mo.
25	M	62	2/8/51	Iliofemoral	Well	60 mo.
26	M	39	3/24/55	Aortoiliac	Well	17 mo.
27	M	48	1/13/55	Aortoiliac	Partial recurrence after 26 mo.	33 mo.
28	M	58	11/6/51	Aortoiliac	Well	4 mo.
29	M	46	1/15/52	Aortoiliac-renal	Well	6 yr.
30	M	49	4/14/55	Left external iliac (graft)	Well	33 mo.
31	M	66	4/2/52	Aortoiliac	Died	1 day
32	M	56	8/30/55	Aortoiliac	Well	27 mo.
33	M	55	11/23/54	Aortoiliac-renal	Died	Surgery
34	M	53	10/11/56	Aortoiliac	Failed	Died 6 wk.
35	M	64	1/9/58	Aortoiliac	Died	Died 2d postoperative day
36	F	61	1/24/47	Aortoiliac	Well	14 mo.
37	M	50	10/18/55	Femoral	Well	9 mo.
38	M	60	3/29/55	Superficial femoral-popliteal	Well	37 mo.
39	F	54	7/2/57	Aortoiliac	Died, rupture	4 mo.
40	M	54	2/2/54	Aortoiliac	Well	44 mo.
41	M	46	12/29/53	Aortoiliac	Well	22 mo.
42	M	45	11/12/53	Aortoiliac	Well	50 mo.
43	F	68	2/6/51	Femoral-popliteal	Recurrence at 16 mo.	6 yr.+
44	M	68	6/26/57	Aortoiliac	Well	8 mo.
45	M	63	2/8/57	Femoral-popliteal	Partial recurrence at 1 mo.	15 mo.
46	M	56	10/25/55	Aortoiliac	Well	19 mo.
47	M	57	10/14/55	Iliac	Well, until death from Ca	Died Ca of lung, 12 mo.
48	F	68	2/24/53	Aortoiliac	Well	54 mo.
49	F	58	6/29/56	Aortoiliac-renal	Well	18 mo.
50	M	49	11/4/52	Aortoiliac	Well, until death from Ca	Died Ca, 54 mo.

* Data on 50 cases, in 49 patients.

Aneurysmal dilatation has not been observed in the remaining cases.

Among the complications in patients operated upon for intermittent claudication, as shown in Table 3, there were four cases of postoperative hemorrhage, one of which was fatal. Cardiac arrest at surgery occurred twice, with one death; and there were seven wound infections, none of which was fatal.

TABLE 2.—*Results of Thromboendarterectomy for Claudication Compared with Those for Ischemia*

	Claudication	Ischemia
Operations	50	37
Mortality	4	3
Immediate failure	2	8
Recurrent thrombosis	7	5
C. V. * deaths up to 3 yr	0	11

* Cardiovascular deaths.

TABLE 3.—*Complications in the Claudication Group as Compared with Those in the Ischemic Group*

	Claudication	Ischemic
Hemorrhage	4—1 death	4—0 deaths
Cardiac arrest	2—1 death	0
Wound infection	7—0 deaths	4—2 deaths
Bowel obstruction	1	0
Thrombophlebitis	2	3

Involvement of a renal artery by the atherosclerotic process with stenosis was present in four patients. In two of these cases this condition was associated with severe hypertension, with a systolic pressure above 240 mm. and a diastolic pressure over 100 mm. Hg. Thromboendarterectomy of the renal artery was performed at the time of the operation on the aorta and iliac arteries. One patient died on the table of a cardiac arrest associated with a massive myocardial infarction. The other three patients recovered, with a satisfactory lowering of their blood pressures. One patient has been followed for over six years, and he still carries a normal blood pressure. Postoperative aortograms in two cases have shown the relief of the stenosis of the renal artery. The result in one case is illustrated in Figure 1.

CASE 49 (Table 1).—A 57-year-old white man presented with claudication and hypertension. Aortoiliac and right renal thromboendarterectomy was done on June 29, 1956. The preoperative film (Fig. 1, left) shows marked stenosis of the right renal artery near the aorta. The postoperative film, on right, shows the cleared artery, with good filling. The patient has been followed to the present time, and has been asymptomatic and normotensive to date.

B. Ischemia.—Thirty-five patients were operated upon because of ischemia, and in two of these patients secondary operations were necessary. The mean age was slightly greater than in the patients operated upon for claudication; for the 21 men it was 67, and for the 14 women, 62.7. The data on these cases are presented in Table 4. In 27 of the 37 cases, or 70% of the cases, operation resulted in the healing of the ischemic lesions and the relief of symptoms. Recurrence of thrombosis occurred in five patients, but in two of these the spontaneous development of collateral circulation prevented the recurrence of their symptoms. Extension of the obliterative arterial disease, or recurrent thrombosis, resulted in amputation in four cases. Salvage of the limb was possible in 29 of the 35 patients.

There were five deaths within the first four months following operation (Table 2), of which three can be considered due to the surgery, giving an operative mortality of slightly less than 10%.

Of great interest is the high incidence of deaths from cardiovascular disease in the

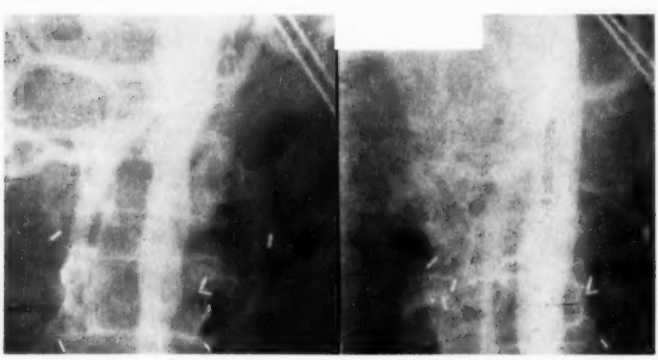

Fig. 1. — Stenosis of right renal artery relieved by endarterectomy.

TABLE 4.—*Ischemia and Claudication* *

Case No.	Sex	Age	Date of Surgery	Operation	Result	Follow-Up
1	F	73	7/12/55	Aortoiliac	Well	43 mo.
2	M	59	7/7/52	Iliofemoral	Healed 16 mo.	Died 17 mo.
3	M	61	6/15/53	Aortoiliofemoral	Healed 7 mo.	Died 8 mo.
4	M	47	10/28/52	Femoral-popliteal	Healed 13 mo.	Died 14 mo., C. V. A.
5	M	70	10/22/55	Aortoiliac	Healed	28 mo.
6	M	70	2/15/55	Iliofemoral-profunda	Healed	39 mo.
7	M	72	2/10/53	Aortoiliofemoral	Healed	Died, heart failure, 2 mo.
8	F	73	7/12/51	Femoral	Failed; amputation 2 mo.	Died, heart, 14 mo.
9	F	79	12/19/56	Popliteal	Well	3 mo.
10	M	57	10/13/53	Femoral-popliteal	Failed; bilateral amputation 2 mo.	Died 18 mo.
11	M	61	12/24/56	Aortoiliofemoral	Well	16 mo.
12	M	80	3/9/55	Iliofemoral-profunda femoris	Well	36 mo.
13	F	56	2/16/55	Common femoral-profunda femoris	Healed	16 mo. Died 19 mo., C. V. A.
14	F	51	9/15/53	Common femoral-profunda femoris	Healed	53 mo.
15	M	74	3/1/51	Femoral-popliteal	? Improvement 4 mo.	Died C. V. A. 16 mo.
16	F	68	1/22/57	Profunda femoris	Failed	Died coronary occlusion, 4 mo.
17	F	74	12/18/52	Femoral-popliteal	Healed	Died C. V. A. 10 mo.
18	M	62	11/17/55	Aortoiliac and left superficial femoral	Improved	25 mo.
19	F	77	10/31/57	Femoral-profunda	Healed and well	5 mo.
20	F	28	8/8/55	Aortoiliac	Failed	Died 6 wk.
21	F	61	1/16/56	Femoral-popliteal	Healed 2 mo., recurred but vessel open 1 yr.	28 mo.
22	M	72	1/1/55	Aortoiliac	Healed	5 mo.
23	M	39	4/6/54	Aortoiliac	Well, but pulseless disease	48 mo.
24	M	58	12/12/52	Iliac	Healed, transmetatarsal amputation	Amputated 2 yr.
25	M	68	1/3/52	Iliofemoral	Failed	Died 6 wk.
26	F	41	2/26/51	Femoral-popliteal	Healed	2 mo.
27	M	70	5/7/53	Femoral-profunda	Well, until	Died 45 mo., coronary occlusion
28	M	56	8/28/56	Aortoiliac	Healed	3 mo.
29	M	53	1/2/53	Aortoiliofemoral	Well, right; failed, left, amputated 3 wk.	57 mo.
30	M	81	1/14/52	Iliac	Healed	62 mo.
31	M	81	3/31/52	Femoral	Healed	60 mo.
32	M	62	11/21/56	Aortoiliac	Failed	Died 10 days
33	M	61	6/27/51	Iliac	Well	Died, coronary occlusion 6 mo.
34	M	59	2/7/52	Aortoiliofemoral	Healed	Died, coronary occlusion 42 mo.
35	M	50	3/17/55	Iliofemoral	Failed, amputation 2 wk.	Died, coronary occlusion 18 mo.
36	F	63	12/29/52	Femoral-popliteal	Recurred, but well	5 yr.
37	F	78	3/7/52	Femoral-popliteal	Healed 6 mo. then recurred	Died 14 mo.

* Data on 37 cases, in 35 patients.

years following operation in these patients who were operated upon for ischemic lesions of their extremities (Table 2). A third of the patients died of cardiovascular disease within the first three years. This figure contrasts sharply with the results in the patients operated upon for intermittent claudication, in whom there were no deaths from cardiovascular disease within the first three years. This difference indicates that there was probably much more widespread obliterative arterial disease in the patients who were operated upon for ischemic lesions of their extremities.

Among the complications, postoperative hemorrhage occurred in four cases, but there were no fatalities (Table 3). Wound infection took place on four occasions, and in two of these patients this infection was associated with recurrence of thrombosis and

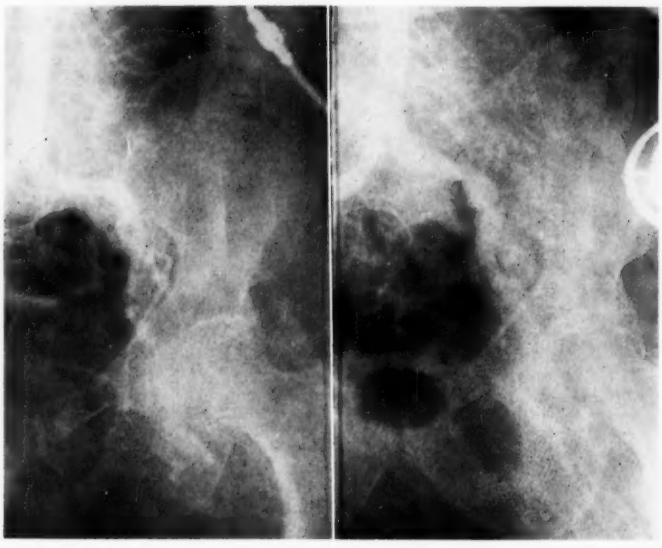

Fig. 2. — Thromboendarterectomy of the femoral and profunda femoris arteries for ischemia.

death. There were three cases of thrombophlebitis.

Of particular interest were the seven cases in which ischemic lesions of the extremities developed after occlusion of the common femoral artery. These patients all had long-standing obliteration of the superficial femoral artery with intermittent claudication, but developed their ischemic lesions only when the common femoral artery was occluded, with obstruction to the deep femoral artery. In six of these patients lasting relief of their symptoms was effected by thromboendarterectomy of the common femoral and profunda femoris arteries (Fig. 2).

Case 6 (Table 4).—Pre- and postsurgical films. A 70-year-old white man had already suffered amputation of his right leg for arteriosclerosis obliterans and gangrene. Left iliofemoral-profunda thromboendarterectomy (Feb. 15, 1955) resulted in prompt healing of an ischemic ulcer. Followed to the present time, he has shown steady improvement, walks with an artificial right limb, and does not even suffer claudication in his usual exercise. He lives alone and looks after his own needs. Figure 2 shows the preoperative aortogram, on the left, with no emptying into the left femoral or profunda femoris artery. On the right, the film shows free emptying into the profunda, although the superficial femoral artery remains blocked.

Comment

The direct surgical approach for the relief of obstruction of arteries due to atherosclerosis obliterans is a new and exciting field, and in selected cases affords very gratifying results. Operation, however, in our hands carries a very definite risk as far as morbidity and mortality are concerned. Whether further experience with this procedure, or the use of some other method, such as the bypass technique using synthetic grafts, will result in a lower morbidity and mortality remains to be seen. It is our feeling that surgery is certainly not the cure for atherosclerosis but may be of great help in the treatment of its complications. Where the process is early and segmental in character, especially with involvement of the aorta and iliac arteries, the prognosis is good, provided that the distal arterial bed is uninvolved. Salvage of the limb can be obtained in a good proportion of the cases provided that the outflow tract is still patent. We at one time advocated the use of regional heparinization following thromboendarterectomy in the hope of maintaining a patent arterial lumen during the process of healing.[4] We no longer feel that this is necessary except in the patients who have a

markedly reduced outflow tract, such as after thromboendarterectomy of the common femoral and profunda femoris arteries.

Even though recurrence of the thrombosis or extension of the process takes place, the operation can be considered to have been successful. We have observed on numerous occasions that the gangrenous process, once stopped by the establishment of a new blood flow to the extremity, does not recur, even though the segment which has been opened up again becomes occluded. It seems likely that the natural process of the development of collateral circulation has furnished a new blood supply which is sufficient to care for the metabolic requirements of the tissues.

Summary and Conclusions

Eighty-seven patients with obliterative arterial disease have been subjected to thromboendarterectomy. In the patients operated upon for claudication, relief has been obtained in 76% of the cases with follow-up from six months to six years. Of the patients operated upon for ischemia, 70% had healing of their lesions or were relieved of their pain. The salvage rate of limbs in this group was 78%.

Morbidity is high in the ischemic group, and the death rate from cardiovascular disease in the early months is also high. Nearly a third died in the first three years.

It is concluded that thromboendarterectomy is a satisfactory operation for the relief of claudication in selected cases. Thromboendarterectomy for ischemic cases should be very carefully considered, in view of the high morbidity and the frequency of early death from cardiovascular disease.

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DISCUSSION

DR. ROBERT R. LINTON, Brookline, Mass.: I have enjoyed these different papers on arterial reconstruction that have been presented this afternoon and have waited to rise to discuss them until they had all been delivered. I will not comment on them individually, but would like to express my present opinions in regard to the various methods which are now available for arterial reconstructive

surgery. I hesitate somewhat to say anything at this time, as I may change my opinions in the next six months to a year, as I have had to do in the past. I think it is worth while, however, to point out that there are five methods of arterial reconstruction for femoral blocks in the lower extremity. These are (1) the venous autograft, (2) thromboendarterectomy, (3) thromboendarterectomy plus the use of a short segment of venous autograft, (4) arterial homografts, and (5) various types of synthetic prostheses. I have given these in the order of my preference at the present time. The reason for putting them in this order is that, in my experience, no venous autograft that was patent on the patient's discharge from the hospital has become occluded after the patient had gone home, and the first one I implanted has now been functioning for eight and one-half years. The most important factor in success in regard to the saphenous vein autograft is that one must learn how to obtain it and implant it, since it is not as easy to handle as the arterial homograft or the prostheses. Originally it fell into disrepute because, at least in our hands, it was always implanted by the end-to-end technique of anastomosis, with a relatively high incidence of early occlusion at the site of anastomoses. At the present time my percentage of success when the saphenous vein autograft is available is much higher than it used to be. The unfortunate thing is that every patient does not have a saphenous vein which can be utilized. The arterial homografts have been very satisfactory, and we have put in many hundreds of them. I think the percentage of immediate success with them is higher than with any other type of graft, but, unfortunately, after they have been implanted for several years, we are beginning to see evidence of late failure, due to thrombosis resulting from aneurysmal dilatation of the homograft. With reference to prostheses, I can state from my own experience that I have put in 12 and the longest that any has remained patent has been two years. The majority have become occluded much earlier than this. These have been of nylon and Ivalon. More recently I have been utilizing the Teflon and Dacron prostheses, and it is hoped that these will function longer; but I am still afraid that as the years go on they will become less pliable, with resulting kinking and obstruction. It is of interest also that we have implanted hundreds of aortic bifurcation homografts in our institution and our initial successes have been very gratifying. Recently, however, we have begun to see evidence of degenerative changes in the iliac limbs of these homografts, an experience which is making me swing over to the prostheses for this type of aortic and iliac reconstructive surgery, especially for aneurysms. In place of grafting procedures for the obliterative lesions of the aorta and iliac arteries, I at present feel that thromboendarterectomy is the best method of treatment. Thromboendarterectomy of the femoral vessels needs further experience in our hands, but I believe it is preferable to any type of arterial replacement other than an autogenous saphenous vein graft. It is a more difficult operation, and I doubt that it will be a generally accepted one except in a few of the vascular centers.

DR. EDWIN J. WYLIE, San Francisco: We have held, and I believe that Drs. Nicholson and Freeman are in agreement, that thromboendarterectomy is the most suitable method of treatment for all operable arteriosclerotic lesions, regardless of their extent or location. Those lesions we now consider inoperable by virtue of the diffuse nature of the disease also seem to be inoperable by other methods.

Initially we were discouraged by our relatively poor results with thromboendarterectomy in the treatment of long femoral artery occlusions. It was soon observed, however, that in cases in which bypass techniques were used there was no greater incidence of long-term success than we had had in our original cases. During the past two years, with the adoption of the internal stripping method, and with a more stringent selection of cases, we have found thromboendarterectomy to be almost as satisfactory for femoral lesions as it had been for aortoiliac lesions. The immediate thrombosis rate following thromboendarterectomy at all sites has dropped to less than 3%. Of 165 patients with initially successful operations, only 2 have developed late occlusion in the segment operated on, if the early group of poorly selected patients having femoral operations is excluded from tabulation. This represents a follow-up period averaging four years and exceeding seven years in many cases. Eighteen occluded femoral arteries have been successfully reopened by internal stripping; all have functioned for an average follow-up period of one year, except for two cases of rupture due to infection in the early postoperative period.

Although I have risen primarily to add further support to Dr. Nicholson's preference for thromboendarterectomy, I wonder whether there might not be a way whereby these conflicts over surgical methods could be resolved. At this and other meetings we have continued to express divergent opinions regarding the most desirable method of treating segmental occlusive lesions of arteriosclerosis. Although the time limitation on our articles tends to restrict these presentations to a parade of results, I feel certain that our data and those of Drs. Nicholson and Linton would be more meaningful if we were to adopt more uniform criteria of evaluation. These would include defining the methods used for selection of cases, comparison of methods only as they apply to similar lesions, and the report of long-term late results as an integral part of the evaluation of the method.

DR. NORMAN E. FREEMAN, San Francisco: I want to say one thing more about the selection of patients for thromboendarterectomy. This operation not only carries some morbidity and mortality but is also expensive to the patient and to the hospital. I have asked the hospital to let me know what the bills were that the patients paid who had undergone thromboendarterectomy. The average for patients with claudication for hospitalization alone, not including special nurses or the professional fee, was $1,000. For those who were being operated on for claudication and for ischemia it was $1,200. This expense may be a serious drain on the patient or his family, and we have to be very careful in the selection of our patients. In my opinion, a simple occlusion of an artery is not an adequate indication for operation. We must take into consideration the need of the patient for the operation. If he is disabled by the claudication, then I think we are justified in operating. If the patient is going to lose his leg otherwise, I think, again, we are justified in operating.

A Study of Grafts in the Venous System

J. F. SCHAUBLE, M.D.; W. G. ANLYAN, M.D., and R. W. POSTLETHWAIT, M.D., Durham, N. C.

Only limited information is available on which to base the selection of grafts suitable for use in the venous system. Grafting techniques have been applied chiefly to the arterial system, and vein grafts have most frequently been studied from the standpoint of suitability as arterial replacements. Nevertheless, patients are seen in whom a graft to replace or bypass portions of the venous system is desirable. Clinical situations encountered include traumatic laceration of major veins, certain arteriovenous fistulae, facilitation of end-to-side portacaval and splenorenal anastomosis, resection and replacement of the superior mesenteric vein in pancreatectomy for carcinoma, benign and malignant vena caval obstruction, and suggested venous shunts to increase compensation in transposition of the great vessels.

This study was undertaken to examine the fate of various types of grafts inserted in the venous system, including fresh autografts, fresh and frozen homografts, and Edwards-Tapp nylon grafts. These grafts were inserted in a site of isogravitational blood flow, such as in the jugular vein and in the femoral vein as a site of antigravitational flow. In addition, the factor of abnormal stasis was studied by inserting the grafts in the femoral veins after vena caval ligation.

Methods

Healthy mongrel dogs, weighing 15 to 30 kg., were anesthetized with intravenous pentobarbital sodium (Nembutal). The recipient site in the jugular or femoral vein was dissected free and stripped of adventitia. After excision of a carefully measured segment of vein, the desired graft was inserted and sutured with continuous, everting 00000 silk, interrupted at two points. The length of the excised segment varied from 2 to 3 cm. Anticoagulant drugs were not used.

The vena caval ligations were performed two to six weeks prior to venous grafting. Light pentobarbital anesthesia was found to be of utmost importance, as deeper levels of anesthesia resulted in death of the animal. The vena cava was doubly ligated with silk just distal to the renal veins. Venous pressures were measured before, during, and regularly for several weeks after ligation. The alterations in venous blood flow characteristics were evaluated by the isotope outflow study, as described by us previously.[3] Briefly, 10μc. to 15μc. of I^{131}-tagged iodopyracet (Diodrast), about 0.5 cc., was injected into the dorsalis pedis vein. The appearance time of the isotope and the curve of the increased radioactivity were recorded simultaneously at the popliteal vein, the femoral vein, and above and below the point of vena caval ligation.

The majority of grafts were equal in length to the segment of replaced vein. Some fresh-frozen homografts, however, though carefully measured, bridged the excised segment only when stretched and narrowed. Accordingly, some grafts were included which were 1 cm. longer in length than the excised vein segment. This variation in length of graft to length of excised segment did not prove of significance to the ultimate success of the grafts, but anastomoses were technically much easier.

Four months after the insertion of the grafts, the grafted segments in the jugular veins were explored surgically. The patency of the femoral grafts was determined by venography. Patent grafts were reexamined at various intervals prior to final excision for histologic study. All occluded grafts were excised for pathologic evaluation.

Results

The results of the 73 grafts in this study are summarized in the accompanying Table. The autogenous vein grafts resulted in the highest percentage of patency at four months, with 80% patency in the jugular veins, 58% in the femoral veins, and 71% in the femoral system after ligation of the

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Results of Eighty-Three Grafts in the Venous System of Mongrel Dogs

Site of Insertion	Autografts		Fresh Homografts		Frozen Homografts		Nylon Grafts	
	No.	% Patent	No.	% Patent	No.	% Patent	No.	% Patent
Jugular	10	80	6	0	12	42	14	0
Femoral	12	58	6	0	8	38	6	0
Femoral-caval ligation	7	71	--	--	--	--	2	0

vena cava. Eight jugular and eight femoral autografts were reexamined from 8 to 12 months postoperatively, and all of these grafts had remained completely patent (Figs. 1 and 2).

After four months' follow-up, 42% of the fresh-frozen homografts in the jugular vein and 38% of those in the femoral vein were patent. None of the fresh homografts remained patent. In contrast to the autografts, the homografts were embedded in dense connective tissue. This striking tissue

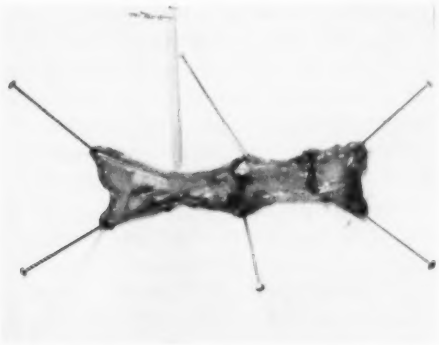

Fig. 1.—Excised jugular autograft after the eight-month follow-up. The graft was completely patent.

response was never seen in the autografts. Patent homografts were often narrowed, and those no longer patent presented as a fibrous cord. The four jugular and three femoral fresh-frozen homografts, which had been patent at 4 months, were all occluded after 8 to 12 months (Fig. 3). All the nylon grafts were occluded at the first postoperative check.

The dogs which had femoral autografts after caval ligation were also part of a series of 25 animals submitted to ligation

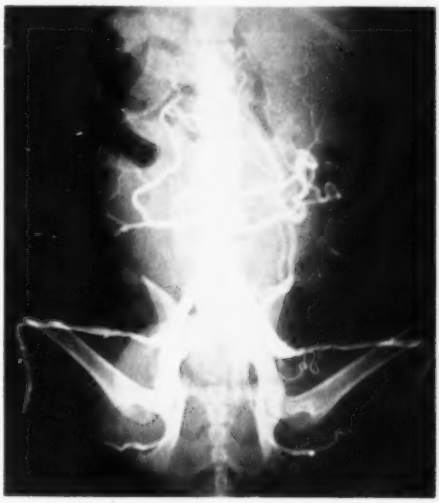

Fig. 2.—Venogram in dog with vena caval ligation and patent autografts in the femoral veins at the four-month follow-up.

Fig. 3.—Venogram showing occluded homografts. Note the extensive development of collateral venous channels around the obstructed segment after several months.

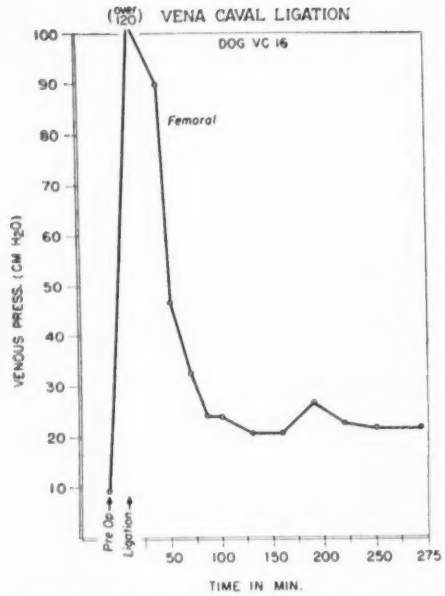

Fig. 4.—Venous pressure determinations in a dog undergoing vena caval ligation.

of the inferior vena cava for certain physiologic observations. Preoperative femoral venous pressures in the animals in this series varied from 4 to 8 cm. of water. Vena caval ligation just distal to the entrance of the renal veins immediately elevated femoral venous pressure to a level ranging from 60 to 100 cm. of water. Within a matter of minutes the femoral venous pressure fell to a range between 25 and 35 cm. of water; it remained at this level over a period of three to four hours (Fig. 4). Three to four months after vena caval ligation, the venous hypertension appeared to be sustained at a level three to four times above the base line preoperative pressure. The vena cava of the dogs of the present series was not the site of extensive thrombosis. Localized occlusion due to the ligation was demonstrated in each case by venography. The persistent relative stasis, despite extensive collaterals seen by venography (Fig. 2), was further documented by the radioactive isotope outflow studies (Figs. 5 and 6).

Comment

Examination of the autograft series showed comparable success with grafts inserted into the jugular and the femoral veins. Although the femoral autograft group did not differ significantly from the other autograft groups, the difference noted in the Table was believed to reflect early technical difficulties at the femoral site, which were resolved as technical experience increased. The fresh-frozen homografts were also successful to the same degree at the jugular and at the femoral sites. Thus, contrary to theoretical expectations, there was no difference in the success between grafts in areas of isogravitational and those in areas of antigravitational flow. It was equally surprising to find that chronic stasis and venous hypertension resulting from vena caval ligation did not influence the success rate of grafts in the femoral veins.

The results in this study are further supported by the experience of other surgeons.

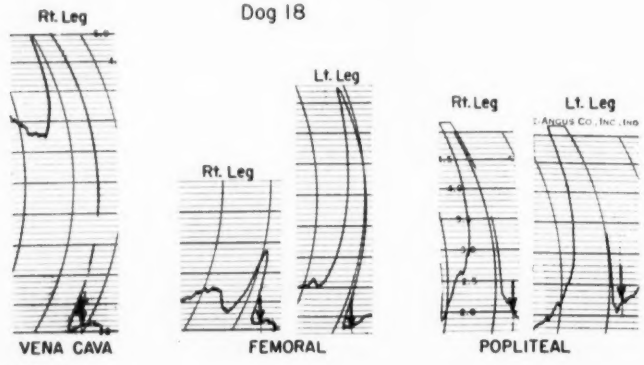

Fig. 5.—Normal isotope outflow study on a dog prior to vena caval ligation. The wave of increased radioactivity at each site was sharp and occurred shortly after the injection of the radioactive iodopyracet (Diodrast) in the pedal vein.

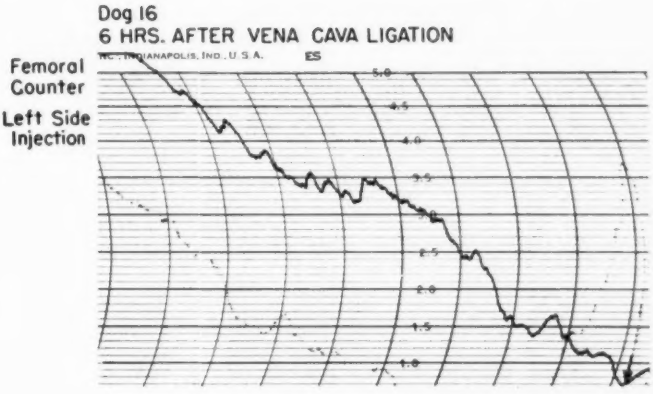

Fig. 6.—Abnormal isotope outflow study following vena caval ligation, showing a delayed and gradual rise in radioactivity at the femoral counter site.

Rousselot [4] reported the successful use of autogenous vein grafts in elongating a short limb in anastomoses between the portal and the systemic circuit in portal hypertension. Sauvage and Wesolowski [5] similarly found a high patency rate of venous autografts in the thoracic portion of the inferior vena cava of growing pigs but found a high failure rate with homografts and plastic prostheses in the same sites. Daniel [3] also reported a high incidence of thrombotic occlusion of plastic grafts inserted in the portal system.

Further study of the factors stimulating or preventing thrombosis of venous homografts and plastic prostheses is needed. The properties that are optimal to maintain patency of plastic grafts in the venous system may be quite different from the qualities desired in the arterial system.

The findings in this study of persistent peripheral venous hypertension several months following vena caval ligation in dogs is not entirely in accord with the report by Dale et al.[2] We were also unable to corroborate his observation of the high mortality rate when the vena cava was ligated just above the iliac veins, in contrast to the low mortality rate with ligation just below the renal veins. No difference in mortality rate existed in our series of 25 dogs between those with high and those with low vena caval ligation.

It is hoped that in the future these findings may be applicable in certain clinical situations, such as traumatic interruption of major veins, localized thrombotic occlusive disease (Fig. 7), extension of short limbs in portacaval or splenorenal anastomoses, superior vena caval obstructions, and transposition of the great vessels.

Fig. 7.—Venogram of patient who had undergone ligation of the external iliac vein for a bullet wound 14 years previously. The defect in the venous system is noted to be localized to the external iliac and common femoral veins.

Summary

The fate of autogenous, homologous, and plastic grafts inserted in the jugular veins

and femoral veins (with and without vena caval ligation) of dogs was studied.

Autografts were equally successful in the jugular system and in the femoral veins (with and without vena caval ligation).

Whereas 42% of the fresh-frozen homografts were patent at the four-month follow-up, all were occluded after eight months. On examination, all were found to be embedded in dense fibrous tissue.

All of the Edwards-Tapp nylon grafts were occluded with organizing thrombi.

Isogravitational or antigravitational flow and stasis did not appear to influence the success rate of the autografts.

Duke University School of Medicine (Dr. Anlyan).

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DISCUSSION

DR. HARRIS B. SHUMACKER, Indianapolis: This paper is open for discussion. Dr. Schauble, I hope in closing you will tell us where you get a suitable autogenous vein to replace a large one.

DR. LAWRENCE: Dr. Shumacker, that is the point for which I arise. I faced a problem a year and a quarter ago in a man who had had a previous bilateral saphenous ligation. He presented with a fibrosarcoma of the right thigh, involving the femoral vessels. A wide en bloc resection was carried out from above the external iliac down to the popliteal vein. (Slide) After reconstitution of arterial flow with a crimped nylon prosthesis (Slide), it became quite apparent that he had intolerable venous hypertension in the lower leg. We elected to put in a crimped nylon graft on the venous side. This functioned very well, as demonstrated by venogram in six weeks. The patient went home with an elastic stocking. He finally abandoned this, when he went back to work. He came to see me a short while ago because of hemoptysis associated with large pulmonary metastases. There was no sign of local recurrence, and he had excellent function in his right leg, without signs of venous insufficiency. However, venography at this time showed that the venous graft had become occluded, the arterial graft remaining patent. This experience supports the excellent experimental work of Dr. Schauble and would indicate that a plastic prosthesis for a vein is indicated only as a short-term expedient when an autogenous graft is not available.

DR. THOMAS C. MOORE: I, too, have enjoyed this very interesting paper by Dr. Schauble and his associates. Our experience in the laboratory supports the superiority of autogenous vascular tissue for venous replacement. While autogenous veins may be employed to replace other veins of equal size, no autogenous vein of sufficient size is available for superior vena caval replacement.

We have been interested in the use of fresh autogenous aorta for superior vena caval replacement. The availability of suitable aortic substitutes, synthetic prostheses, and homografts makes it possible to obtain segments of fresh autogenous aorta. Fresh autogenous aorta, used for superior vena caval replacement, was found by us to remain patent and free of thrombosis formation and narrowing in all of 33 dogs studied up to one year after operation.

We are also investigating the usefulness of alcohol-preserved heterografts of cow carotid artery for superior vena caval replacements in dogs. Although the heterografts in the superior vena cava in these animals were patent in all of three dogs studied by cavogram 12 months after placement, significant narrowing was encountered in one segment of the heterograft in the one animal which was killed after the cavogram was taken.

An Evaluation of Newer Opacification Media

Diatrizoate and Diprotrizoate

THEODORE B. MASSELL, M.D.; E. CRAIG HERINGMAN, M.D., and S. M. GREENSTONE, M.D., Los Angeles

The opacification of blood vessels for radiographic visualization, long a common diagnostic procedure in Western Europe and Latin America, was not widely adopted in this country until relatively recent years, following the development of direct surgery of the arteries. More frequent intravascular injections of radiopaque substances have been followed by a disturbing increase in reports of serious sequelae.[2,3,5,11,13] Some of these untoward reactions have been due to the technique of injection, but most have been properly attributed to the opacification media.[1,3]

Previously [8] we reported our experience with one of the new contrast media, diatrizoate, in about 100 vascular opacifications. Since then we have continued the study with the diatrizoate salts and have made parallel observations with sodium diprotrizoate.

Chemistry

The chemical structures of diatrizoic acid and diprotrizoic acid are similar (Fig. 1). Each is a 2, 4, 6-triiodobenzoic acid nucleus with an acid amino side-chain in the 3,5-position. These side-chains differ only in the presence of one CH_2 group. An aqueous solution of a soluble salt is used. Two diatrizoate solutions are available: Either the sodium salt (Hypaque Sodium) or a mixture of methylglucamine and sodium salts (Hypaque M; Renografin). Only one form of diprotrizoate is used, the sodium salt (Miokon Sodium). The three salts have essentially the same iodine content. Chemically these are comparable to the older organic iodine compounds, such as iodopyracet (Diodrast) and acetrizoate (Urokon), but pharmacologic studies in animals indicate that both diatrizoate and diprotrizoate are considerably less toxic than iodopyracet or acetrizoate.[6,16]

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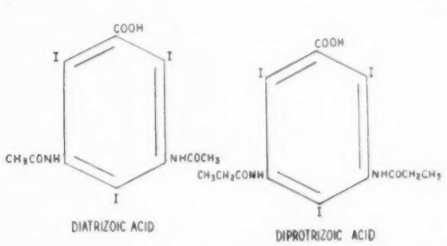

Fig. 1.—Chemical structure of diatrizoic and diprotrizoic acids. Both are triiodobenzoic acid compounds and differ only in the length of the 3, 5 side-chain.

Plan of Study

For the purpose of our clinical study, observations were made on 230 patients. Injections for the purpose of opacifying blood vessels were performed in 229 cases. One patient developed severe generalized urticaria after a test dose of diatrizoate sodium, so that a projected phlebography was abandoned. Because many patients had bilateral extremity disease and others required the visualization of more than one area, the total number of injections was 308. The distribution of patients and injections according to the type of procedure is indicated in Table 1. Usually multiple injections in one patient were made with the same medium in order to avoid confusion regarding the agent responsible for any late untoward systemic reactions. In four cases, however, the initial injection of one medium caused such severe local pain that a different material was used for contralateral injection.

The only anesthetic required in most cases was a small amount of procaine infiltrated along the course of the needle, through which the opaque medium was subsequently injected. However, nine of the peripheral arteriograms were obtained by

TABLE 1.—*Types of Vascular Opacification*

Medium	Aortogram		Peripheral Arteriogram		Phlebogram	
	Patients	Injections	Patients	Injections	Patients	Injections
Diatrizoate sodium	4	4	32	41	32	39
Mixed diatrizoates	27	33	18	26	36	48
Sodium diprotrizoate	5	7	18	28	58	82
Total	36	44	68	95	126	169

cut-down on anesthetized patients to confirm the presence of an open outflow before placing an aortic graft. One patient insisted upon a spinal anesthesia before she would consent to aortography. During all the other injections the patients were awake and alert to describe any discomfort.

Aortography

Forty-four aortograms were performed on 36 patients. All but one were by translumbar puncture of the abdominal aorta, using a single 17-gauge, thin-walled needle. The exception was a left common carotid cut-down with the use of a polyethylene tube threaded into the aortic arch. In many of the translumbar aortographies the femoral vessels were exposed simultaneously on a second film.

Only one of the three agents, the mixed diatrizoate salts, gave consistently satisfactory opacifications of the aorta, iliac, and femoral arteries. Diatrizoate sodium solution was not available in concentrations higher than 50%, and at this dilution the opacification was too faint even in cases with obstructive lesions. The mixture of methylglucamine and sodium diatrizoate was available in concentrations up to 90%. However, the optimum strength in our experience was about 75%. The more concentrated solutions were so viscous, even when warmed to body temperature or slightly higher, that the rate of injection became too slow. As little as 15 cc. of the 75% solution usually gave excellent opacification of the aorta and iliac arteries in patients of average size. In order to overcome the effect of dilution, as much as 35 cc. was used when it was desirable to include the femoral and popliteal vessels of large patients.

Sodium diprotrizoate was unsatisfactory for aortic opacification despite the availability of concentrations up to 90%. The opacification by the more dilute solutions seemed too faint, and the viscosity of the more concentrated solutions prevented sufficiently rapid injections. If we had used a larger needle than 17T, or two needles of this size, or a high-pressure injection device, we could probably have achieved more intense opacification of the aorta with this medium. However, we found it unnecessary to increase the hazards of the procedure by using any of these devices, since the results with the mixed diatrizoates were so consist-

Fig. 2.—Lumbar aortogram with 30 cc. of 75% solution of Renografin, performed because of known iliac occlusion. The small aneurysms of the lumbar aorta and left common iliac artery were not apparent on physical examination.

TABLE 2.—*Opacification Intensity with Media Used in Aortography*

Medium	Patients	Injections	Opacification: Excellent	Good	Unsatisfactory
Diatrizoate sodium	4	4	0	0	4
Mixed diatrizoates	27	33	19	10	4 *
Sodium diprotrizoate	5	7	0	2	5

* At least two of these unsatisfactory results were the result of technical errors in the procedure.

ently good (Fig. 2). Our results with the different media are summarized in Table 2.

All three preparations were very well tolerated by the patients. Only one patient complained of pain, which persisted about one minute after the injection of 25 cc. of 75% solution of mixed diatrizoates. This was a very small woman with considerable aortic and iliac obstruction and poor outflow tracts. The pain, however, was not severe enough to cause motion. Several other patients described a transient feeling of warmth or heat in the abdomen or groins, which was not painful. The majority of the patients were not even aware of the injection. This was a striking and welcome contrast to the effects of acetrizoate and iodopyracet. When these substances were used in the past without general or spinal anesthesia, few patients were able to avoid writhing in pain.

The absence of serious, and even of mild, systemic reactions was also striking. One patient had an episode of coughing and vomited after the injection of 35 cc. of 75% solution of mixed diatrizoates. This was the only overt systemic reaction observed.

Four patients showed very heavy opacification of renal or visceral arteries without any ill effects. One case seemed especially significant. The patient was a short, heavy, 57-year-old woman, with bilateral femoral artery occlusion and clinical evidence of narrowing at the aortic bifurcation. The needle was introduced into the aorta at the level of L-2. However, after the scout film, the needle was accidentally advanced so that the tip was at the orifice of the right renal artery. Thirty-five cubic centimeters of 75% solution of mixed diatrizoates was injected, most of it entering the right renal artery. The abdominal film is reproduced in Figure 3. The needle was repositioned below the renal arteries, and another injection, of 25 cc., of the solution was performed. For 24 hours afterward there were casts in the urine; albumin was present for 48 hours. Thereafter the urine became normal. Phenolsulfonphthalein excretion and the blood urea nitrogen level 24 hours after the injection were both within normal limits. Seven weeks later intravenous urography was performed, which indicated unimpaired excretory power in the previously injected right kidney (Fig. 4).

Fig. 3.—Abdominal film after accidental injection of 75% Renografin into the right renal artery. It is estimated that almost 30 cc. of the medium went through the right kidney.

Since most of the aortography was performed with the diatrizoate solutions, the number of injections of diprotrizoate was too small to permit any conclusions regarding its tolerance. Nevertheless, one case,

Fig. 4.—Intravenous urogram using 50% diatrizoate (Hypaque) sodium solution, performed seven weeks after the accidental renal artery injection illustrated in Figure 3.

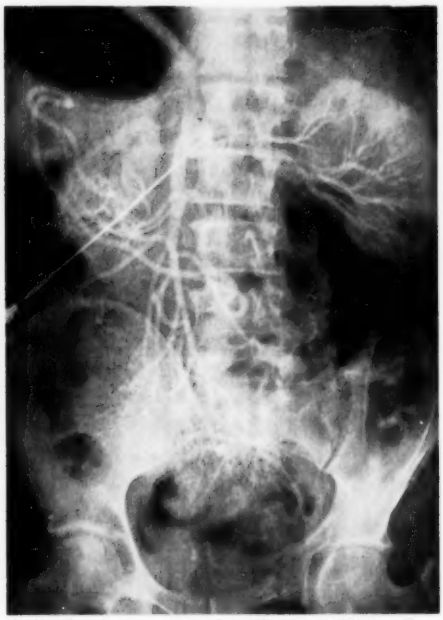

Fig. 5.—Aortogram using 25 cc. of 75% sodium diprotrizoate (Miokon) solution. Injection was made just above a fresh thrombus of the lumbar aorta.

illustrated in Figure 5, was of significance. This is the abdominal film obtained after injecting 30 cc. of the 70% solution into the aorta above a recent, rather acute thrombosis. Despite the heavy opacification of the superior mesenteric and renal arteries, the patient manifested no ill effects.

In aortography the largest single injection was 26.5 gm. of diatrizoate salts, and the largest total dose was 45.5 gm.

Arteriography

Peripheral arteriography was performed 95 times on 68 patients, all with lower-extremity disease. All injections were made in the femoral artery in the groin, usually with an 18-gauge, thin-walled needle. Six arteriograms were obtained in cases with aneurysms or arteriovenous fistulas; the remainder were in arteries which were either narrowed or occluded distal to the injection. The amount of the contrast medium varied from 7 to 12 cc. of 50% solution, except for the mixed diatrizoates, which were packaged in 60% solution and used at this concentration in a correspondingly decreased volume. All three agents produced satisfactory opacification, although the diatrizoate solution seemed somewhat better than the diprotrizoate, as indicated in Table 3. Actually, the poorer results with the diprotrizoate were due to pain and motion, not to less intense opacification. In our earlier report[8] we thought that the mixed diatrizoates gave more intense opaci-

TABLE 3.—*Opacification Intensity with Media Used in Arteriography*

Medium	Patients	Injections	Opacification		
			Excellent	Good	Unsatisfactory
Diatrizoate sodium	32	41	32 (78%)	9 (22%)	0
Mixed diatrizoates	18	26	20 (77%)	6 (23%)	0
Sodium diprotrizoate	18	28	19 (68%)	6 (21%)	3 (11%)*

* The results in all three cases were unsatisfactory because of motion secondary to pain caused by the injection of the contrast agent.

TABLE 4.—*Untoward Reactions with Media Used in Peripheral Arteriography*

Medium	Injections	Local Anesthesia	Involuntary Motion	Pain			Distal Spasm	Systemic Reaction
				Severe	Moderate	Mild		
Diatrizoate sodium	41	34	4 (12%)	4 (12%)	6 (18%)	9 (26%)	0	0
Mixed diatrizoates	26	26	0	0	8 (31%)	4 (15%)	0	0
Sodium diprotrizoate	28	26	3 (12%)	5 (19%)	4 (15%)	5 (19%)	2 (8%)	1 (4%)

fication than the sodium salt but that apparent difference was not corroborated as the series increased.

Untoward reactions from the use of diatrizoate were almost entirely local and transient (Table 4). One patient manifested syncope, pallor, coldness of the extremities, and a weak pulse for several minutes after the injection of 8 cc. of 50% sodium diprotrizoate. Another patient had pallor, wheezing, and itching after the intravenous injection of a 1 cc. test dose of sodium diprotrizoate but had no systemic reaction when the arteriography was performed with mixed diatrizoate salts.

Some local pain in the arteries distal to the injection site was rather common—in about 45% of injections with mixed diatrizoates and in 55% with diatrizoate sodium or sodium diprotrizoate. However, there was a striking difference in the severity of the pain, when present. It was never severe with the mixed diatrizoates despite the use of a 60% solution, whereas severe pain was noticed in 12% of injections with diatrizoate sodium and in 19% of those with the sodium diprotrizoate. Involuntary motion due to pain occurred in four cases (12%) following the use of diatrizoate sodium and in three cases (12%) with diprotrizoate. Visible spasm of distal vessels was observed in only two instances, both following the use of diprotrizoate, one despite the fact that a lumbar sympathetic block with procaine had been performed shortly before the intra-arterial injection.

Phlebography

The largest group of vascular opacifications comprised the phlebograms, consisting of 169 injections in 126 patients. The technique has previously been described by us.[7,9] Usually 20 to 25 cc. of 30% solution was used, although a few trials were made with smaller volumes of concentrations up to 50%.

Because of uncontrollable variations in tissue density, injection rates, and venous patterns, it was not feasible to rate the intensity of opacification more accurately than as good or unsatisfactory. The results are summarized in Table 5. All three media seemed to produce good opacification. Several of the cases rated as unsatisfactory were due in part to technical difficulties either in the injection or in the radiography.

TABLE 5.—*Opacification Intensity with Media Used in Phlebography*

Medium	Patients	Injections	Good	Unsatisfactory
Diatrizoate sodium	32	39	37 (95%)	2 (5%)
Mixed diatrizoates	36	48	41 (85%)	7 (15%)
Sodium diprotrizoate	58	82	70 (85%)	12 (15%)

Likewise there were no serious reactions after phlebography with any of the three preparations. Even mild systemic reactions were uncommon. One patient exhibited coughing and vomiting after the injection of diprotrizoate; two had nausea without emesis. One incident of nausea followed the use of each of the other two media. There were three mild cases of urticaria: two after diprotrizoate and one after diatrizoate sodium. There were also two reactions to the test dose: one case of urticaria from diatrizoate sodium and one instance of nausea from mixed diatrizoates. In the latter case there was no reaction to a sub-

TABLE 6.—*Untoward Reactions with Media Used in Phlebography*

Medium	Injections	Local Pain and Spasm			Systemic	
		Severe	Moderate	Mild	Nausea	Urticaria
Diatrizoate sodium	39	5 (13%)	11 (28%)	3 (8%)	1	1 (5%)
Mixed diatrizoates	48	1 (2%)	1 (2%)	8 (17%)	1	0 (2%)
Sodium diprotrizoate	82	13 (16%)	14 (17%)	6 (7%)	3	2 (6%)

sequent test dose of diprotrizoate, but there was some nausea after the injection of the opacification dose. If one considers the incidence of untoward systemic effect in cases in which there was no reaction to the test dose, the mixed diatrizoates with 2% would possibly seem safer than diatrizoate sodium with 5% and sodium diprotrizoate with 6%. However, if one includes the reactions to the test dose, it is apparent that mild untoward reactions may be anticipated in something over 5% of all patients with any of the three contrast agents.

The striking difference among the three preparations was in the local reactions, indicated in Table 6. Severe pain and spasm followed the injection of mixed diatrizoates in only 2% of cases, diatrizoate sodium in 13%, and sodium diprotrizoate in 16%. Qualitatively, the difference between the diatrizoate sodium and the sodium diprotrizoate seemed greater than indicated by the statistics, inasmuch as pain was accompanied by significant movement three times after the injection of the diprotrizoate, whereas there was no observable motion following any of the diatrizoate phlebographies. Four patients who required bilateral phlebography experienced such severe and prolonged pain after an initial injection of diprotrizoate that diatrizoate sodium was used for the other leg in three of the cases, with much less discomfort, and mixed diatrizoate solution was used in the fourth case on the contralateral side, with only mild pain.

Outward manifestations of vasospasm, such as pallor and decreased pedal pulses, often accompanied the severer incidents of pain, but there were no late sequelae, such as venous or arterial thrombosis.

Comment

In an earlier report, we suggested the need for further experimental studies with animals to elucidate the effects of intravascular injections of critical doses of diatrizoate salts. Thomson and co-workers [15] have reported that diatrizoate and diprotrizoate are less injurious to the kidneys of dogs than acetrizoate and iodopyracet. Other studies [6,16] indicate similar findings. Further experimental work with larger series of animals is still required to explore all possible toxic effects of these newer materials.

In this series both compounds seemed free of serious effects in doses large enough for eminently satisfactory opacification of vessels in human patients. This impression gains further corroboration from the fact that the reports of serious sequelae of vascular opacifications continue to implicate acetrizoate, iodopyracet, and the inorganic iodides.[10] The mixed methylglucamine and sodium salts of diatrizoate are already being used for vascular opacifications outside the United States on the basis of lessened chemotoxic effects,[14] and two favorable reports have already appeared in recent American literature.[4,12]

Of the three preparations, the mixed salts of diatrizoate appear definitely to be the best, inasmuch as the solution causes the least local reaction in smaller arteries and veins and produces the best opacification in the aorta. That solutions of pure sodium salts are more irritating in small vessels than the solutions containing an admixture of methylglucamine salts is suggested by the similarity in local effect of the diatrizoate sodium and the sodium diprotrizoate. However, the diprotrizoate molecule itself seems

more irritating than the diatrizoate, and at this time the use of sodium diprotrizoate for vascular opacification appears indicated only in those patients who react unfavorably to a test of the diatrizoates. The addition of a methylglucamine radical to sodium diprotrizoate might well increase the usefulness of this preparation.

Summary

Three hundred eight vascular opacifications were performed by the injection of the following media: diatrizoate sodium (Hypaque Sodium), sodium and methylglucamine diatrizoate (Hypaque M; Renografin), and sodium diprotrizoate (Sodium Miokon).

There were no serious untoward reactions. Systemic reactions were mild and occurred in only 2.9% of the cases.

None of the preparations caused pain when injected into the aorta. The mixed diatrizoate salts produced mild or moderate pain in some cases when injected into smaller arteries or veins, but this was rarely severe and never persistent. Either preparation of the pure sodium salt would occasionally cause severe pain in the small vessels, the diatrizoate being less irritating than the diprotrizoate. All three agents produced excellent opacification in the peripheral vessels. Only the mixed diatrizoate salts were consistently good for aortic opacification. The diatrizoate solution, specifically the mixture of methylglucamine and sodium diatrizoate, is recommended to replace the older, more toxic vascular opacification media, such as acetrizoate and iodopyracet. The optimum dosage and concentrations appear to be (1) 20 to 35 cc. of a 75% solution for aortography; (2) 7 to 12 cc. of a 60% solution for peripheral arteriography, and (3) 20 to 25 cc. of a 35% solution for peripheral phlebography.

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Acute Cholecystitis

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The surgical treatment of acute cholecystitis remains a controversial issue, but, as time goes on, it is being more widely accepted as the policy of choice.

In general, there are three views: (1) Early surgery should be undertaken shortly after the diagnosis is established and the electrolyte and fluid balance corrected, regardless of the time elapsed since the onset of the condition; (2) early operation should be performed only if the patient is seen early in the attack, but operation should be postponed and conservative treatment carried out for the patient seen 72 hours or later after the initiation of the acute attack, and (3) all patients should be treated conservatively, surgery being postponed either until the acute process subsides or until it is evident that perforation is imminent.

In recent years many surgeons have placed increased emphasis on the importance of early operation in acute cholecystitis. Early surgery should be differentiated from emergency surgery, and may be defined as surgery performed shortly after the diagnosis is established and the fluid and electrolyte balance corrected.

Early surgery presumes that the patient's general condition has been rendered suitable for surgery, that a surgeon is present who is experienced in surgery of the biliary tract, and that adequate assistance and facilities are available. Within the first 48 to 72 hours after the onset of acute cholecystitis, operation can be accomplished with approximately the same degree of difficulty as operation for chronic cholecystitis. After this period, the inflammatory process in the tissues results in somewhat increased difficulty for the surgeon, but the experienced surgeon, with care, can execute the operation safely.

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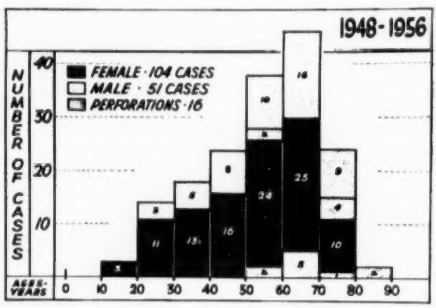
Present Study

In this paper, we propose to present our experience with 155 consecutive cases of acute cholecystitis treated surgically, after a short period devoted to diagnosis and correction of the fluid and electrolyte balance.

In the nine-year period from Jan. 1, 1948, to Dec. 31, 1956, we operated on 155 consecutive patients with acute cholecystitis in three hospitals in Fort Wayne, Ind. The gallbladders of 16 of these patients were perforated at the time of surgery.

The age and sex distributions by decades are presented in the Chart. The youngest patient was 18 years of age, and the oldest 89. The ages of 101 patients were under 60 years, and those of 54 were over 60. In this series, acute cholecystitis was most frequent in the sixth and seventh decades of life. Of these patients, 104 were women and 51 were men.

Stones were present in the gallbladder in 154 cases, and stones occurred in the common duct in 19 cases (Table 1). In one case stones were present neither in the gallbladder nor in the common duct. The incidence of acute cholecystitis in the ab-



Age and sex distribution of acute cholecystitis.

TABLE 1.—*Incidence of Stones, Jaundice, and Pancreatitis*

Incidence of stones	
Stones in gallbladder	154
Stones in gallbladder and common duct	19
No stones in gallbladder and common duct	1
Incidence of jaundice	
Jaundice present	23
Jaundice absent	132
Incidence of pancreatitis	
Pancreatitis present	9
Pancreatitis absent	146

sence of stones in this series is less than that reported by several authors.

In 23 cases obstructive jaundice was present, an incidence of approximately 15%. Pancreatitis was present in nine cases, as evidenced by elevation of the serum amylase and confirmed by surgery (Table 1).

In 144 cases cholecystectomy was performed (Table 2). Eleven patients were considered to be unsuitable for this procedure, either because they were too ill or because the local findings rendered the procedure too hazardous. In these 11 patients cholecystectomy was performed. Four of the latter procedures were performed under local anesthesia. In 36 of the patients who were subjected to cholecystectomy, choledochostomy was also performed, because of the history of recent jaundice, operative findings, or operative cholangiographic findings. In 19 of these cases stones were found. There were no cases in this series in which cholecystectomy and choledochostomy were performed, although

TABLE 3.—*Cholangiography*

Cholografin		17
Gallbladder	Not visualized	15
	Visualized	2 *
	Stones	3
Common duct	Not visualized	2
	Visualized	15 †
	Stones	0
Operative cholangiography		12
Normal		10
Stones		2

* Questionably visualized.
† Poorly visualized.

TABLE 2.—*Operative Procedures*

Cholecystectomy		144
Cholecystostomy		11
General anesthesia	7	
Local anesthesia	4	
Cholecystectomy and exploration of common duct		36
Cholecystostomy and exploration of common duct		9

this combined operation is an acceptable procedure.

In 17 cases, iodipamide (Cholografin) studies were made (Table 3). In 15 cases nonvisualization of the gallbladder was observed; in 2 cases there was questionable visualization. In 3 instances stones were observed in a nonfunctioning gallbladder. In 15 cases the common duct was visualized; in 2 cases there was no visualization. No stones were observed in the common duct in this series. This procedure has proved to be a valuable adjunct in the diagnosis of acute cholecystitis.

In 12 cases operative cholangiography was utilized (Table 3). In 10 cases the common duct was normal. In 2 cases stones were discovered in the common duct which otherwise would have been overlooked. We feel that this procedure is at times a helpful adjunct to cholecystectomy, and it appears that it can be performed in the presence of infection without risk.

There were nine deaths in this series (Table 4). Five of these occurred in cases with perforation, in one of which the patient had a late perforation and was in very poor condition. In retrospect, this patient should probably not have been subjected to surgery. Five patients died of peritonitis; one died of uremia; one died after a pulmonary embolus; one died of cardiac failure, and one died as a result of coronary thrombosis.

TABLE 4.—*Causes of Death*

Peritonitis	5
Uremia	1
Pulmonary embolus	1
Cardiac failure	1
Coronary thrombosis	1

TABLE 5.—*Mortality Rates*

	Cases	Deaths	Percentage
Perforations (16) included—155 cases			
Under 60 yr.	102	2	2.0
Under 70 yr.	139	4	2.9
Over 70 yr.	16	5	31.9
Total	155	9	5.8
Perforations (16) excluded—139 cases			
Under 60 yr.	98	2	2.0
Under 70 yr.	129	2	1.5
Over 70 yr.	10	2	20.0
Total	139	4	2.8

The total mortality in the series is 5.8% (Table 5). If the cases of perforation are excluded, the mortality is reduced to 2.8%. There were no deaths in patients under 50 years of age. If the cases of perforation are included in the series, the mortality under 60 years of age is 2%, under 70 years 2.9%, but over 70 years, 31.9%. If the cases of perforation are excluded, the mortality is 2% under 60 years, 1.5% under 70 years, but 20% over 70 years.

Comment

The view that early surgery is the preferential method of treatment of acute cholecystitis has, in recent years, gained many supporters. Sanders,[1] Heuer,[2] Glenn,[3] and Hotz[4] share this view. This policy prevents the development of gangrene and perforation, and eliminates the recurrent attacks characteristic of this disease. It must be remembered that conservative treatment merely tides the patient over the acute episode and leaves him, after a prolonged illness, with the original disease and with the prospect of future attacks, still requiring definitive surgery.

The danger from unexpected perforation alone is a very strong argument for early surgery in acute cholecystitis. Diffenbaugh,[5] in a series of 5,272 cases of acute cholecystitis collected from the literature, found the average incidence of perforation to be 11.9% and the average mortality 23.8% (Table 4). It is not generally appreciated that the incidence and mortality of perforation in acute cholecystitis is so high. The difficulty in differentiating acute cholecystitis from empyema and gangrene of the gallbladder in the older age group is well known. It is equally difficult to distinguish acute cholecystitis from a walled-off abscess which has resulted from perforation of a gangrenous gallbladder. Very often the patient appears to be improving clinically, whereas the diseased gallbladder has progressed to gangrene and perforation.

The diagnosis of acute cholecystitis can be established with considerable accuracy. A routine EKG and chest x-ray will rule out myocardial infarction and pulmonary and pleural disease. If the EKG should be equivocal, transaminase determination will frequently exclude myocardial infarction. Roentgenograms of the abdomen in the upright and lateral decubitus positions will establish the absence of air under the diaphragm and will be of value in ruling out a perforated viscus.

Normal serum amylase determinations will rule out the presence of acute pancreatitis. Frequently a degree of pancreatitis will accompany an episode of acute cholecystitis. Moderate elevation of the serum amylase may also be observed in cases of perforated peptic ulcer, and occasionally in superior mesenteric thrombosis.

Intravenous iodipamide studies will assist considerably in establishing the diagnosis of acute cholecystitis. Nonvisualization of the gallbladder and visualization of the common duct are frequently observed. In those patients who are able to take oral medication, nonvisualization of the gallbladder may be confirmed by routine cholecystography.

A serum bilirubin determination will reveal, occasionally, a not too apparent jaundice and indicate the necessity for exploration of the common duct. The incidence of stones in the common duct in acute cholecystitis varies from 10% to 25%.

It is our contention that, in most instances, surgery can be carried out at any time after the diagnosis is established and

the fluid and electrolyte balance restored within normal limits. This can usually be accomplished within 24 hours. The operation is usually scheduled on the morning following establishment of the diagnosis and correction of the electrolyte and fluid balance. This is usually the morning following the day of admission to the hospital.

The operation of choice is cholecystectomy. Usually, in the hands of an experienced surgeon, assisted by good anesthesia and the use of muscle relaxants, it presents little difficulty. Cholecystectomy will be greatly facilitated if the bile and stones are evacuated prior to dissection of the cystic artery and cystic duct. Sometimes this procedure is not feasible, either because of the patient's general condition or because of the local findings. Under such circumstances, cholecystostomy may be used to good advantage, as a compromise procedure, since it can be done with minimal risk to the patient and will also protect him from the common complications. In many poor-risk cases, cholecystostomy is best performed under local anesthesia. Frequently the life of a poor-risk patient can be salvaged with this technique.

When indicated, exploration of the common duct is carried out, in addition to cholecystectomy or cholecystostomy. The addition of this latter procedure, we feel, need not add materially to the morbidity or mortality of the operation.

Operative cholangiography is frequently a useful adjunct to surgery. Contrary to the common belief that this should not be done in the presence of infection, we have encountered no complications attributable to this procedure. Unsuspected stones in the common duct may be disclosed, as well as residual stones left after common-duct exploration.

The higher mortality rate in the group over 50 years of age, as contrasted with the group under 50, is significant. It indicates the desirability of reducing the number of operations in the older age group.

Obviously, acute cholecystitis cannot be prevented after the age of 50, but the incidence can be materially reduced if those patients with acute cholecystitis are operated upon in the first attack and if all patients with cholelithiasis are subjected to cholecystectomy when they are first discovered.

Summary

A series of 155 consecutive cases of acute cholecystitis, in which early surgery was performed without regard to the interval between the onset of the disease and the performance of surgery, is presented.

The diagnosis can be established with considerable accuracy if the outlined routine is followed.

Cholecystectomy is usually the procedure of choice. Cholecystostomy is occasionally indicated, sometimes under local anesthesia in poor-risk patients.

Operative cholangiography is frequently a helpful adjunct and can be performed without any deleterious effects on the patient.

Under 50 years of age the mortality is low; over this age the mortality rises sharply.

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First-Day Removal of Skin Sutures

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The closure of a skin incision following either surgery or trauma is often as varied a procedure as the number of men performing it. Since any method usually achieves eventual closure of the skin, irrespective of its final appearance, an attempt was made to reduce this procedure to the simplest form possible without changing any surgeon's individual technique. Acknowledging that the healing power inherent in the skin itself is the one factor common to all, to utilize this to its utmost with as little interference as possible should improve the final result. This healing process is initiated with the first stroke of the scalpel and proceeds to its termination in a day-to-day orderly process that refuses to be hurried. Requiring only two surfaces capable of union, this procession of events will usually continue as long as they are in apposition. Any foreign body interposed between these surfaces slows, stops, or interferes with these reactions until it is removed. It was presumed that sutures or clips, while necessary in the initial approximation, were in themselves foreign bodies, no matter how inert. Then, too, these agents often retard healing when they are too tight by producing local areas of necrosis, and, when too loose, are insufficient to bring about the needed adherence. While it is known that these agents can serve as a means of introducing infection, they can provide a continuing pathway for infection as long as they are in place. It is also a known fact that suture marks often remain glaringly in evidence, while the incision scar becomes almost invisible.

Present Investigation

Material and Methods.—In view of all this, it was decided that an effort would be made to evaluate the necessity of skin-closure agents beyond the first 24 hours following the completion of surgery. Knowing that a good fascial closure is the essential factor in holding the incision together, it was decided to remove all skin sutures and clips within the first postoperative 24 hours, thereafter keeping skin edges approximated with adhesives only, and then to compare these incisions with those repaired in the usual fashion. As a control, each case so treated would be compared with a similar case treated in the conventional manner at about the same time, so that the two cases could be watched simultaneously. In the case of bilateral herniorrhaphy, one side would act as the control side; the other, as the treated one. No selection as to the type of patient or the type of incision was made. All cases were hospitalized patients (outpatients were not used in order that observations could be maintained constantly), selected in the consecutive order of admission.

Various methods and materials for fascia and skin closure were utilized, according to the usual procedure of the operator's choice, except that no subcutaneous sutures above the fascia were used in any of the treated cases. No cases in which retention sutures were applied through the fascia and skin were included in this survey; however, many such cases were treated and used for observation purposes only. Incisions over flexor or extensor surfaces were excluded, because of excessive strain on the incision line.

Two hundred cases were used in this series, all of which had skin-closure agents removed within the first 24 postoperative hours. Following this, adhesive butterflies were used to keep the skin edges in apposi-

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tion, and the patient was allowed to resume the usual postoperative routine with no unusual exceptions or restrictions. Wherever possible, removal of the skin-closure material was accomplished within the first 12 hours except where the skin edges exuded some blood, in which case the sutures or clips were removed between the 18th and the 24th hour. No case was considered in this series where the skin-closure material remained in place for more than 24 hours from the time surgery was completed. All cases with drains were included, regardless of how long the drain had to remain in place. No age group was exempted, nor was evidence of any other disease a disqualifying factor.

The butterfly dressings were applied about 1 in. apart and left undisturbed during the entire hospital stay except for an occasional replacement or addition in weakened areas. In uncomplicated cases the patient was discharged in the usual time, which was about 7 to 10 days on the average. At home the patient was allowed a shower on the third or fourth day to help remove the adhesive, or it might be allowed to remain in place until the first postoperative visit. No further dressing or other care was used.

A list of the operations performed follows.

Appendectomy (including operation for appendicitis with perforation)	38
Hernioplasties (inguinal, umbilical, ventral, epigastric)	46
Cholecystectomies	23
Gastrectomies	9
Colon resections	10
Abdominoperineal resections	4
Mastectomies (simple, radical)	6
Ligation of varicose veins	12
Removal of skin tumors (including breast)	21
Exploratory laparotomies	11
Thyroidectomies	12
Traumatic wounds	8
	200

Fifty-six of these patients, or 28%, had their sutures or clips removed within the first postoperative six hours. Sixty-four, or 32%, had everything removed within the second six hours. Eighty, or 40%, had them removed between the 12th and the 24th postoperative hour.

Results.—No wound dehiscence occurred in any of these cases. All incisions healed promptly with no evidence of delay, since no foreign material was present to interfere.

In none of the cases was there any sign of infection, either superficial or in the deeper subcutaneous tissues. No gauze dressings were used over the incisions after removal of the sutures or clips except while drains were in place. These top dressings were removed once all wound discharge had ceased. It was felt that once the skin had sealed itself, maceration due to perspiration was prevented, and with no path for infection to enter, the incision was much better protected. Superficial stitch infections occurred in 10% of the controls, with four deep-wound infections. No reaction to adhesive was noted in this group, but it is to be presumed it may occur in a larger series and some other type of reinforcement might be needed.

Uniformly, the patients stated that they felt little discomfort without sutures or clips in place, and none of the pulling sensations experienced with the other methods. This was probably due to the fact that there was no traction by the skin against an inelastic material in its substance, since all pressure was completely superficial. Patients with bilateral inguinal hernia unequivocally stated that the side with sutures and clips in place felt more uncomfortable than the counterpart. Discomfort was very common in the control group.

The removal of all sutures and clips in this early period was found to be a much easier and relatively painless procedure. Most of the patients were still somewhat subdued from the premedication and anesthetic and consequently noticed little sensation. Then, too, no fibrous tissue had formed about the sutures in this short time to incorporate them solidly into the area.

Cosmetically, it was felt that the shorter the time the sutures or clips remained in

place the better the final appearance of the incision. No patient was found to have suture or clip marks present more than 48 hours after removal, and the less time these materials remained in the skin the faster these marks disappeared. The line of the incision itself was usually thin and a light pink in color. During the follow-up period (which has been a year in some of the cases only, owing to the fact that many are being followed by their respective surgeons outside the hospital) these incision scars were generally found to be narrower and much less noticeable than the controls.

Summary

Two hundred operations of various types were performed in which all sutures or clips were removed within the first 24 postoperative hours. Two hundred similar cases were selected to act as controls.

All incisions in the treated group healed promptly and with fewer complications than did those in the controlled, or untreated, group.

Patients had less wound discomfort without sutures or clips in place than did those treated by the usual methods.

No skin infection was found in any of the treated cases.

Cosmetically, the appearance of the skin was superior to that in cases repaired by the usual method.

Butterfly adhesive dressings were sufficient to keep the wound edges in apposition during the entire postoperative period.

Removal of sutures and clips in the early postoperative period is considered to be a definite all-around improvement over the usual method of allowing them to remain in place for longer periods.

Addendum

Since these first cases were studied, one wound dehiscence has occurred, as a result of disruption of the rectus fascia. This was noticed on the second postoperative day as a small piece of bowel bulging into the incision at its base and was repaired at once. The convalescence was uncomplicated from this point on. It was felt that with the usual method this dehiscence would not have been found until about the seventh postoperative day, necessitating a longer period of hospitalization and further risk to the patient.

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Biliary Tract Disease Following Billroth II Subtotal Gastrectomy

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The development of gallbladder disease in some of our patients who previously had subtotal gastrectomies has been noted. Most of these procedures were performed for complicated duodenal ulcers and have been the Billroth II (Polya-Lahey modification) type of anastomosis. It is in general acceptance that upon the entrance of fatty food and gastric secretions into the duodenum, this part of the intestine, and also the upper jejunum, liberates a hormone, called cholecystokinin, which will produce contraction of the gallbladder and, at the same time, relaxation of the sphincter of Oddi.[3] After a gastrectomy with a Billroth II type of anastomosis, the anatomy of the stomach and proximal intestine is completely changed, and fatty food or gastric secretions will not come in contact with the duodenal mucosa; however, ingestion of a fatty meal by a gastrectomized person following a preparation with iopanoic (Telepaque) tablets causes varying degrees of contraction and emptying of the gallbladder, as observed in x-ray.

On the other hand, much has been written on the fact that major surgery, particularly when the use of gastric suction and the administration of a considerable amount of narcotics have been necessary, will cause inhibition of the gallbladder and also spasm of the sphincter mechanism of the lower common duct. This produces stagnation of bile in the extrahepatic biliary system (10 mg. of morphine sulfate raises the pressure within the common duct from 0-2 mm. of H_2O to 200-300 mm. of H_2O).[5] Schwegman and De Muth[4] reported 14 cases of acute cholecystitis following operations of unrelated disease, 2 of them following gastrectomies. Probably this complication was due to forceful contractions of the gallbladder in response to ingestion of food after a period of bile stagnation.

Most of the biliary calculi are produced by precipitation of cholesterol. The cholesterol content of liver bile is from 0.04%-0.16%, and it goes up to 0.2%-0.5% after concentration of bile in the gallbladder. The ratio of concentration of cholesterol in bile to that of bile salts is from 1:20 to 1:30. If the ratio falls to 1:13, precipitation of cholesterol occurs.[1]

According to Gardner,[2] the cholesterol of bile does not vary with changes of total blood cholesterol, nor is its concentration raised by increasing the cholesterol content of the diet. It continues to be excreted upon a cholesterol-free diet. Certain forms of renal disease and myxedema are accompanied by hypercholesteremia and yet show no evidence that this will cause cholelithiasis. During pregnancy the normal proportion of free cholesterol and esters of cholesterol is altered. These abnormalities in cholesterol metabolism may have more importance in the formation of stones. In the present study of gastrectomized patients, the blood was analyzed for both cholesterol and esters of cholesterol in 16 cases. The percentage of esters of cholesterol from total cholesterol varies from 77 to 60, with an average of 71.

This study was done to determine whether or not gastrectomy increased the incidence of biliary tract disease. A total of 173 gastrectomies were performed on sur-

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gical service B at the Lankenau Hospital from January, 1951, through December, 1955. Of these patients, 130 were men and 43 were women. One hundred forty-four patients were followed from three to seven years; six had a cholecystectomy prior to their gastrectomy, and three at the time of gastric resection. Of the remaining 135 cases, 7 had gallbladder surgery following the gastrectomy (5.18%)—2 for chronic calculous cholecystitis, 2 for chronic noncalculous cholecystitis, and 2 for acute cholecystitis (1 case, two and one-half weeks after gastric resection; 1 case, one month after gastric resection). The remaining case is known to have had a cholecystectomy elsewhere.

Twenty-one of these cases of subtotal gastrectomies were studied. All of the operations were performed for complicated duodenal ulcers. There were 15 men and 6 women. The studies consisted of clinical evaluation; cholecystography, including determination of responses to a fatty meal, and blood analysis for cholesterol and esters of cholesterol.

One of these cases presented pain in the upper abdomen; five, belching; two, fat intolerance; five, flatulence; three, nausea; one, vomiting, and five, bile regurgitation; there was no jaundice. None of these patients gave the impression of having gallbladder disease, and their dyspeptic symptoms had the appearance of being referred to postgastrectomy sequelae.

Five patients had considerable loss of weight, but none of them presented a nutritional problem. Two of them presented nutritional imbalance, but this condition had existed prior to gastrectomy. One patient gained weight, and the others had no considerable change.

Eleven of these cases had cholecystograms in the Lankenau Hospital prior to gastric resection. In all but one case good concentration of the dye was found at that time. Of these 11 patients, 7 showed good concentration of the dye in the present cholecystogram; 2 presented a lower concentration on the present cholecystogram than on the previous one. In only two cases was there a definite decrease in the concentration of dye, and in one of these gallbladder disease was proved on laparotomy. The other case was a 68-year-old, apprehensive woman whose only complaint was of bile regurgitation, and who otherwise did not present any symptoms to suggest gallbladder disease. Her cholecystogram showed poor concentration of dye but a normal response to a fatty meal.

Of these 21 cases, 11 presented good concentration on the oral cholecystogram, 5 had moderate concentration, 3 had poor concentration, and 2 presented no visualization of the gallbladder. These last two patients are completely asymptomatic and have had excellent results after gastrectomy. Of the three cases with poor concentration of dye, two had normal responses to fatty meals; the third did not have a fatty meal during the x-ray study but is completely asymptomatic. In 12 of the 21 cases the cholecystogram included x-ray pictures following a fatty meal, and in all of them normal responses were demonstrated with contraction of the gallbladder to at least one-half its previous size.

The blood was analyzed for total cholesterol and esters of cholesterol. They were all within normal limits.

Summary and Conclusions

This study was performed to find out whether or not gastrectomy with the Billroth II type of gastrojejunostomy would cause impairment of the function of concentration and emptying of the biliary system. The clinical study, cholecystogram, and serum cholesterol of the cases do not give any evidence of impairment of the extrahepatic biliary system, in spite of the bypassing of the duodenum and upper jejunum by food and gastric secretions. The incidence of biliary dysfunction after this type of operational procedure is no greater than that of the general population, or that of patients who have undergone any other type of abdominal surgery.

1. Twenty-one gastrectomized patients were studied, with reference to their history, physical examination, cholecystogram, and serum cholesterol.

2. One of these patients underwent cholecystectomy for subsiding acute cholecystitis three months after gastrectomy. None of the other patients presented symptoms or signs of gallbladder disease.

3. Cholecystography in most of these cases did not prove any definite impairment in the function of the gallbladder, and those in which it did demonstrate impairment had normal responses after a fatty meal. Two cases had no visualization of the gallbladder, but both of these are completely asymptomatic.

4. Serum cholesterol, including esters of cholesterol, were all within normal limits. Of the 135 cases of gastrectomized patients, 7 needed surgery of the biliary system.

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The Reliability of Palpation for Common Duct Stones

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Introduction

This investigation was undertaken to demonstrate the degree of accuracy with which stones can be palpated in the extrahepatic biliary ducts. It was prompted by the following considerations:

1. Our clinical impression that palpation of the ducts, when carefully and thoroughly performed, is reliable for determining the presence or absence of stones.

2. A suspicion gained from reports in the surgical literature that this impression is not shared by many of our colleagues. Diffenbaugh and Strohl [1] state that "a stone can be palpated in approximately one-fourth of those ducts containing stones." Waugh, Johnston, and Cain [2] found palpable stones in only 45 (25.7%) of 173 patients with common duct stones.

3. An opinion based on repeated observations that palpation of the biliary ducts, as commonly practiced, often is incomplete and restricted to the supraduodenal portions of the ductal system.

This project was initiated in 1952, and the succeeding 400 unselected and consecutive patients undergoing biliary tract surgery were the subjects of the study. Operations were performed by residents and staff members alike, each operator first having been indoctrinated in the manipulations and observations required. In every instance, the second portion of the duodenum was mobilized by division of its lateral peritoneal reflection in order that the retroduodenal portion of the common duct and the ampulla of Vater might be included in a meticulous palpation of the entire extrahepatic biliary system (Figure). This method of mobilization of the duodenum was described by Kocher [3] in 1903 as a maneuver to facilitate the performance of the Billroth I gastric resection and has since borne his name. It has subsequently proved to be of great value in surgery of the common bile duct.

If stones were palpated, or if one or more of the other accepted indications for choledochotomy was present, the common duct was opened and explored. Findings with respect to contained stones were compared with those recorded on palpation prior to opening the duct. In each case in which choledochotomy was performed, thorough palpation of the duct was repeated after intraluminal manipulation had been concluded, and before insertion of the T-tube and closure of the duct. Postoperative cholangiography served as a final check on the accuracy of palpation for detecting retained stones.

Results

Indications for exploration of the common duct were adjudged to be present in 83, or 20.7%, of the 400 cases comprising this study. These indications are listed in Table 1. Fifty-one, or 61.4%, of these patients presented more than one indication for choledochotomy.

In 28, or 33.7%, of the choledochotomies stones were found and removed. These stones were palpated prior to opening the duct in all but one case, an accuracy of 96.4%. The indications for choledochotomy in these 28 positive explorations are tabulated in Table 2. In three cases, the sole indication for opening the duct was the presence of a palpable stone. It is inter-

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Kocher maneuver as used for palpation of the retroduodenal portion of the common bile duct.

esting to note that dilatation of the common duct, which has been reported by Baker [4] as one of the most reliable indications for choledochotomy, was present in only 53% of our positive explorations. However, this apparent discrepancy is not surprising when one considers the wide variation in the "normal" size of the common duct and the degree to which the individual operator's interpretation enters into the diagnosis of dilatation.

In many instances it was possible to predict by palpation the exact number and dimensions of the stones which were found. In 21 cases the findings recorded prior to opening the duct, when compared with the exploratory findings, were gratifyingly accurate. These data are shown in Table 3.

TABLE 1.—*Indications for Choledochotomy in Eighty-Three Cases*

Indication	No. of Cases	Per-centage
Multiple small stones in gallbladder	53	63.9
Jaundice, or history of same	47	56.6
Dilated common duct	30	36.1
Palpable stones in the ducts	29	34.9
Associated pancreatitis	5	6.0
Noncalculus gallbladder with "typical" attacks of biliary colic	4	4.8
Aspiration of muddy bile	2	2.4

TABLE 2.—*Indications for Choledochotomy in Twenty-Eight Positive Explorations*

Indication	No. of Cases	Per-centage
Palpable stones	27	96.4
Dilated common duct	15	53.0
Small stones in gallbladder	14	50.0
Jaundice, or history of same	13	46.4

TABLE 3.—*Comparison of Findings on Palpation and on Exploration*

Case No.	Stones Palpated	Stones Removed
1	1	1
2	2	2
3	1	1
4	1	1
5	Many	22
6	Many	9
7	1	1
8	5	5
9	1	1
10	2	2
11	Many	8
12	2	2
13	1	1
14	1	1
15	1	1
16	3	3
17	4	4
18	Many	13
19	2	2
20	1	1
21	Many	5

In the remaining six cases the findings on palpation were either inaccurate as to number of stones or indefinitely recorded so as to be considered inaccurate.

In one case there was a single small stone found which was not palpated prior to opening a dilated duct. Nodules in the head of the pancreas were mistaken for stones and accepted as an indication for choledochotomy in two of the negative explorations. Thus, the rate of false-positive interpretations for palpation of stones in the choledochotomy cases was 6.9% and of false-negative interpretations, 1.8%.

Postoperative cholangiograms revealed retained stones in 2 (2.4%) of the ducts explored. These stones were confirmed in each instance by reoperation for their removal. In one other case in which no stone was palpated and none was found on choledochotomy performed for another indication, one equivocal and one negative postoperative cholangiogram were obtained. The T-tube was removed. One year later the patient reported a three-day illness characterized by abdominal pain and jaundice. Subsequent examinations, including liver function studies and intravenous cholangiography, were negative. The patient has remained asymptomatic for the ensuing one and one-half years. It is believed that this attack of painful jaundice was due to a retained stone, which may or may not have been passed at the time of the episode. If the case is accepted as such, it increases the percentage of retained stones to 3.6% in this series.

For 317 of the 400 cases included in this study choledochotomy was not performed. We have been able to obtain recent reports from 176 of these patients, in spite of the obvious difficulty of following an ever-moving service personnel and their dependents. In only one instance have postoperative events pointed to an undetected common duct stone. Curiously enough, this stone was easily palpated prior to opening the duct for its removal at a second operative procedure.

We have not encountered postoperative complications which could be related specifically to the manipulative procedures associated with kocherization of the duodenum and careful palpation of the extrahepatic biliary ducts. There were three deaths in the series, for a mortality rate of 0.75%. Two deaths occurred in poor-risk patients with acute cholecystitis and complicating disease. One death was the result of secondary hemorrhage from the hepatic artery.

Comment

The reported incidence of choledochotomy at time of cholecystectomy varies considerably. On the average, approximately one-fourth of the ducts are opened. Through a six-year period, 1946-1951, 24% of the common ducts of patients undergoing gallbladder surgery at the Mayo Clinic [5] were explored. Stones were found in 46% of the explored ducts, for an over-all incidence of 11%. Other series show considerable variation in the percentages, as shown in Table 4.

In respect both to percentage of ducts explored and to incidence of stones found the figures from this study are somewhat lower than the average. However, the incidence of undetected stones in those cases in

TABLE 4.—*Incidence and Results of Choledochotomy*

Series	No. of Cholecystectomy Cases	Percentage Ducts Explored	Percentage Explored Ducts Positive for Stone	Percentage Over-All Incidence of Duct Stones
Strohl, et al. [13]	900	18	53	9.6
Ochsner [14]	468	28	39	11.5
Colcock and McManus [15]	1356	36.7	28	10.5
Adams and Stranahan [16]	1104	45	36.9	16.8
Babcock and Eyerly [18]	1055	24	55.0	12.9
Authors	400	20.7	33.7	7.0

which the duct was not opened has been minimal (one case), as judged by follow-up data to date. It is interesting to note that if palpation of stones in the ducts had been used as the sole indication for choledochotomy in this series, only 7.3% of the ducts would have been explored but the over-all incidence of stones found would have remained essentially the same, 6.8%.

No complete solution has been found to the problem of the retained common duct stone. McKittrick,[6] in 1949, reported an enviable incidence of retained stones of only 2%. He did not use operative cholangiography. Other comparable figures, as collected by Corff,[7] are shown in Table 5 and range from McKittrick's low to a high of 24.3%.

Much has been written on the advantages and disadvantages of operative cholangiography as related to this problem. Some authors take the stand that it is of great value, while others feel that if this procedure is to assume a place of importance in the exclusion of stones, the accuracy of the procedure must be increased. Kantor, Evans, and Glenn [8] reviewed 171 operative cholangiograms and 234 postoperative cholangiograms, all made in a study of 158 common-duct explorations performed between 1947 and 1952. They reported an incidence of retained common duct stones of 9%, with an "unsatisfactory result" in 48% of the operative cholangiograms.

TABLE 5.—*Retained Stones—Without Operative Cholangiography*

Author	Year	No. of Cases	Percentage Retained Stones
McKittrick, Boston	1949	100	2
Buxton, University of Michigan	1948	439	5.9
Waugh, Mayo Clinic	1954	175	8
Hicken, Salt Lake City	1954	550	20
Hughes, Cleveland	1948	90	24.0
Preston, Wilmington, Del.	1955	74	24.3

The question as to whether operative cholangiography has reduced the incidence of retained stones in the experience of a single operator is an intriguing one. Unfortunately, few such comparative studies can be found in the literature. Corff [7] reported a series of choledochotomies in 1952 in which only 34% had operative cholangiography. The incidence of retained stones was 18%. He compared this in 1955 with a series of 100 cases with 100% operative cholangiography. There was a 10% retention of stones. While this is an 8% reduction in the incidence, it is still an appreciable retention rate. Paine and Firme,[9] in 1954, reported a similar comparative study, with a reduction in the incidence of retained stones of from 28% to 22%.

Wall and Peartree [10] reported a series of 444 patients subjected to operative cholangiography with an over-all diagnostic accuracy of 88%. In 63 patients stones were revealed on operative cholangiography. In 36 of these patients the common duct had been explored and judged to be free of stones. Of these 36 patients, the retained stones lay within the common duct in 24 and within the hepatic ducts in 12. The ducts were reopened and in all but two patients the stones removed. In those two patients the stones were high in the hepatic ducts and could not be extracted. In both

these cases postoperative cholangiograms showed that the stones had dropped down in the ducts, and they were removed at a subsequent operation. Certainly, it is difficult to argue against this secondary, or postcholedochotomy, type of operative cholangiography when it can be shown to have saved 34 patients the necessity of a second operation for retained stones. However, one cannot but wonder at the exceedingly high incidence of false-negative ductal explorations. Is it possible that the operator who is depending upon operative cholangiography to ascertain the presence of retained stones after exploration may be less meticulous in the manner and persistence with which he pursues exploration prior to resorting to the use of the x-ray?

There has been considerable written about the incidence of acute pancreatitis following surgery on the extrahepatic biliary system, particularly after exploration of the common duct. Thompson, Howard, and Vowles,[11] in a recent article, reviewed the literature on this subject and collected 75 cases with this complication following biliary tract surgery. In over 90% of these the operative procedure had included choledochotomy. The mortality has been 77%. We have not encountered this complication following the rather extensive manipulation of the head of the pancreas and common duct practiced in our cases. However, it is worthy of note that, in several instances, mild to moderate pancreatitis was observed as a complication of the routine postoperative cholangiography.

In conclusion, we believe that we have demonstrated that meticulous palpation of the entire extrahepatic biliary ductal system, as outlined, is an extremely valuable and accurate method for demonstrating stones, both as an indication for choledochotomy and to minimize the incidence of retained stones. Our figures for the latter compare very favorably with those reported by exponents of operative cholangiography.

Summary

This investigation was undertaken to demonstrate the degree of accuracy with which stones can be palpated in the extrahepatic biliary ducts. Four hundred unselected and consecutive cases of biliary tract surgery provided the clinical material. In every instance the second portion of the duodenum was mobilized by division of its lateral peritoneal reflection in order that the retroduodenal portion of the common duct and the ampulla of Vater might be included in a meticulous palpation of the entire extrahepatic biliary system.

The common duct was opened and explored for the commonly accepted indications. Findings with respect to contained stones were compared with those recorded on palpation prior to opening the duct. In each case in which choledochotomy was performed, thorough palpation of the ducts was repeated after intraluminal manipulation had been concluded, and before insertion of the T-tube and closure of the duct. Postoperative cholangiography served as a final check on the accuracy of palpation for detecting retained stones.

Indications for opening the common duct were present in 83 (20.7%) of the 400 cases included in the study. In 28 (33.7%) of the choledochotomies stones were found and removed. These were palpated prior to opening the duct in all but one case, for an accuracy of 96.4%. In many instances it was possible to predict the exact number and dimensions of the stones which were found. Nodules in the head of the pancreas were mistaken for stones and accepted as an indication for choledochotomy in two of the negative explorations.

Postoperative cholangiograms revealed retained stones in two (2.4%) of the ducts explored. These stones were confirmed in each instance by reoperation for their removal. In one other case an attack of painful jaundice one year postoperatively has been attributed to a retained stone, although subsequent studies, including intravenous cholangiography, were negative and the pa-

tient has remained asymptomatic for the ensuing one and one-half years.

In only 1 of the 317 cases in which choledochotomy was not performed (176 of which have recently been followed) have subsequent events pointed to an undetected common duct stone. Curiously enough, this stone was easily palpated prior to opening the duct at a second operative procedure.

These results are offered in evidence that meticulous palpation of the entire extrahepatic biliary ductal system, as outlined, is an extremely valuable and accurate method for demonstrating stones, both as an indication for choledochotomy and to minimize the incidence of retained stones.

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Repair of Tendon Injuries in the Hand

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Fibrosis is the greatest enemy of function in the hand. It causes skin to be adherent to bone, and to be prone to easy ulceration with trauma. It makes the injured nerve either completely nonconducting or the cause of severe pain. It grows between fractured ends of bones, to result in nonunion. But its greatest and most easily recognized insult to the structures of the hand is manifested after injury to tendons. If extensive scarring occurs, or even if minimal scarring grows from the healed tendon to inelastic structures, the tendon will not glide.

Some fibrosis from the laceration is inevitable. Our aim is to minimize this reaction, and not to add to it.

Natural Causes of Fibrosis

The natural causes of fibrosis are (1) injuries to tissue: lacerated, crushed, and avulsed; (2) exposure of raw tissues to any environment but skin; (3) hematoma formation; (4) lymph pocketing; (5) edema, and (6) infection.

Any trauma to tissues results in some fibrosis. The severer the trauma the more extensive is the ensuing scarring. Thus, if the tissues are deeply abraded and/or crushed, the trauma is severer than with a laceration. However, if the tissues are left open for hours or days, extensive fibrosis is inevitable. The presence of blood or lymph pockets will result in capsule formation of scar tissue even if the fluids are later drained off. The extraordinary pressure of edema results in a diminished blood supply. The edematous areas are replaced with scar. The anoxia of a stagnant blood supply results in widespread scar.

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Surgical Procedures That Increase Scarring

Traditional surgical methods which increase fibrosis follow.

1. Scrubbing raw tissues with chemicals: tinctures and modern germicides
2. Soaking in antiseptics and "healing" solutions
3. Leaving wounds open to "granulate in," or to grow bed of "granulations" for graft
4. Operative desiccation of tissues
5. Use of excessive amount of large suture material
6. Huge drains for prolonged drainage
7. Uncontrolled edema
8. Immediate or early motion "to prevent adhesions"

Most of the traditional surgical errors of commission are listed above. Most of them are tragic. Prolonged soaking of raw tissues in any man-made solution for days or weeks maintains an altered homeostasis, with chronic low-grade, or even acute, infection. The scarring is severe. To leave the wound open to fill in is, by definition, fibrogenic. Drying of tissues, such as is often seen in prolonged orthopedic procedures, is as deadly to tissues as is a blowtorch. The layers of air-dried dead cells in the operative site will be replaced by binding scars.

Techniques That Minimize or Prevent Scarring

Fibrosis may be minimized or prevented by the following techniques:

1. Cleansing raw tissue with mild white soap and water

2. Gentle handling of tissues
3. Maintenance of moist state during surgery
4. Complete hemostasis
5. Use of few fine sutures
6. Immediate or early skin cover
7. Layer-by-layer repair
8. Compression dressing
9. Adequate splinting

Therefore the general rules for minimizing the amount of scar in the hand, as we know them now, are basically to treat the living tissue as living tissue. It is to be handled gently and to be kept moist with saline constantly throughout the operative procedure.

Suture Technique

The long flexor tendons and the extensor tendons proximal to the dorsal carpal ligament are closed with special techniques in order to afford maximum holding power with minimal postconvalescent scarring. These use the well-known Bunnell [1] wire and the Mason [2] silk sutures. They are used in the special instances of long flexor tendons severed anywhere distal to the musculotendinous junctions and for long extensor tendons severed proximal to the distal edge of the dorsal carpal ligament and distal to the musculotendinous junctions. Both schools close the intrinsic muscle tendons and the long extensor tendons distal to the dorsal carpal ligament with simple sutures of 000000 silk.

These special suture techniques—the wire and the silk—are used with success by those who are familiar with them. Although I use the Mason suture in these special instances, I feel that the results are the same as with the wire sutures and that those surgeons who are obtaining good results with either technique should not change. It is not the technique but, rather, the technician that makes for functional results.

Sutures are not made, nor are they intended, to hold tendon ends together under tension. If there is any tension, they will break or slough through. The suture is intended simply to align the tendon ends. The position of the splinted hand relaxes the muscle of the severed tendon and prohibits contracture. The most important rules to remember are to treat the tissues gently and to splint the hand in such a position—marked flexion or extension, as indicated by the site of trauma—that the patient cannot flex or extend the ray further.

Anatomical Precautions

One should note the volar surface of the hand and wrist, in any textbook of anatomy,[3] especially the "pulleys" or annular ligaments. If the tendon anastomosis is allowed to rest against the cut surface of these unyielding tissues, there will be no motion in the healed tendon. Similar immobility results when the anastomosis rests against raw bone which has suffered open injury or fracture. Therefore, only fat, gliding tissue, adventitia, or muscle may be placed in contact with the anastomosis. Although the tendon will heal or fuse to this tissue, the tissue will stretch and permit motion.

The dorsal structures of the hand are treated similarly, with avoidance of unyielding proximities, except that the simple suture is used by adherents of both schools to anastomose severed parts of the extensor mechanism.

Fig. 1.—Laceration through flexor digitorum profundus, showing activity after healing.

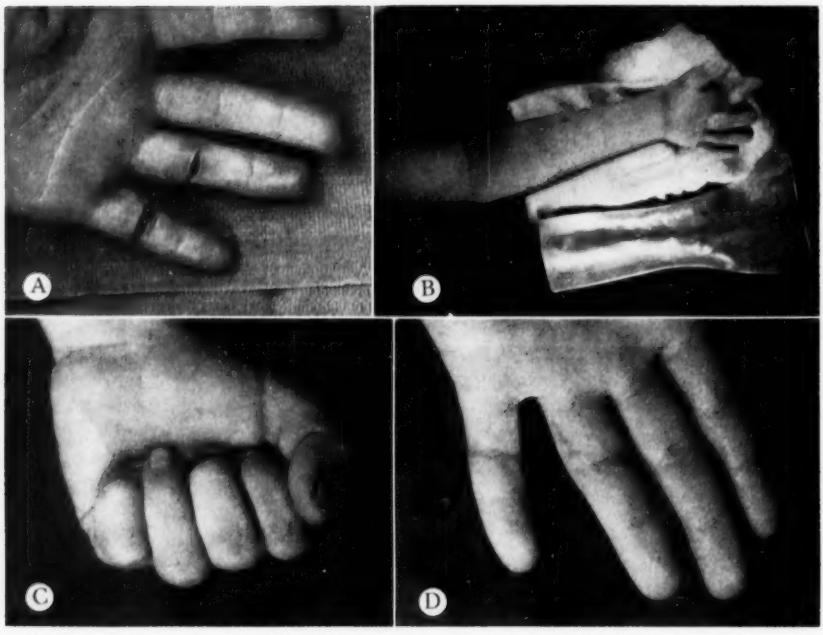
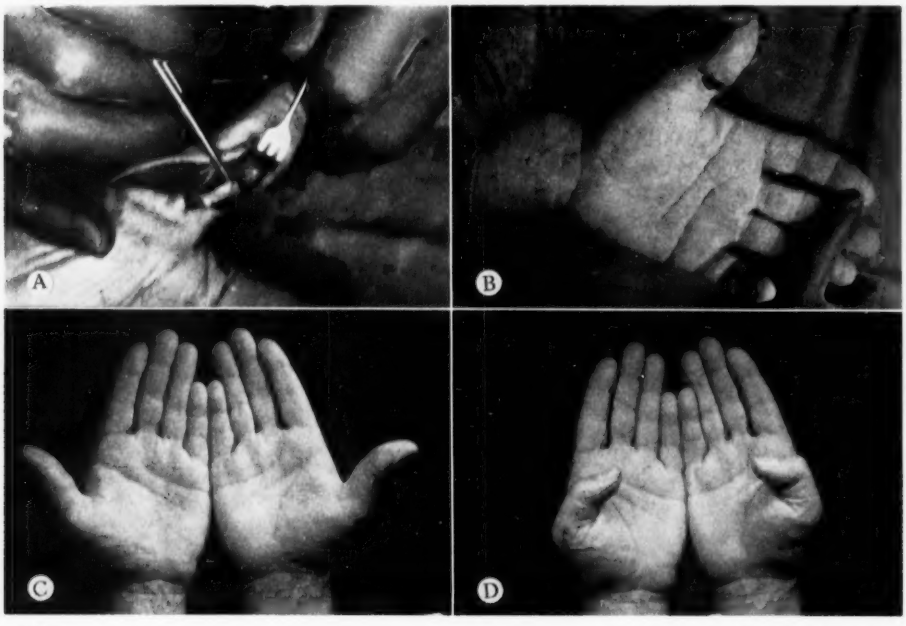


Fig. 2.—Lacerations of both long flexor tendons to two fingers, showing splint. *D*, lateral extensions of the lacerations to facilitate exposure.

Fig. 3.—Laceration of flexor pollicis longus and lateral volar thenar nerve, with degree of active motion in four months.



Representative Tendon Injuries

The following representative cases are taken from a series of 43 tendon repairs.

Figure 1*A* shows the laceration through which the flexor digitorum profundus tendon was cut. The short transverse laceration was inadequate to permit exposure of the tendon ends, and hence was enlarged by extending it distally on the radial side, and proximally on the ulnar side, of the finger. It was sutured with the Mason tendon suture technique. *B* shows extension, and *C*, flexion, in four months.

Figure 2*A* shows the two lacerations through which the flexor tendons to the ring and little fingers were severed. The flexor digitorum sublimis tendon was removed from each finger, and only the profundus tendons were repaired by the Mason suture. *B* shows the hand just removed from the padded splint. *C* shows flexion in three months, and *D*, extension. Sensation—normal.

In Figure 3*A* the flexor pollicis longus tendon was cut with the volar digital nerve on the radial side of the thumb. In *B* the proximal end of the tendon has been pulled within ⅛ in. of the distal part after the laceration had been enlarged by a lateral incision. *C* reveals extension in five months; *D* shows nearly normal flexion. Sensation—normal.

Figure 4*A* illustrates a laceration of the long extensor tendons to the first three fingers. Little was seen of the actual structures that were injured until the laceration was enlarged by a *Z*, or bayonet, type of incision (Fig. 4*B*). It should be noted, too, that extension of the wrist helps bring the severed tendon ends into view. The tendons were anastomosed with simple sutures in this instance

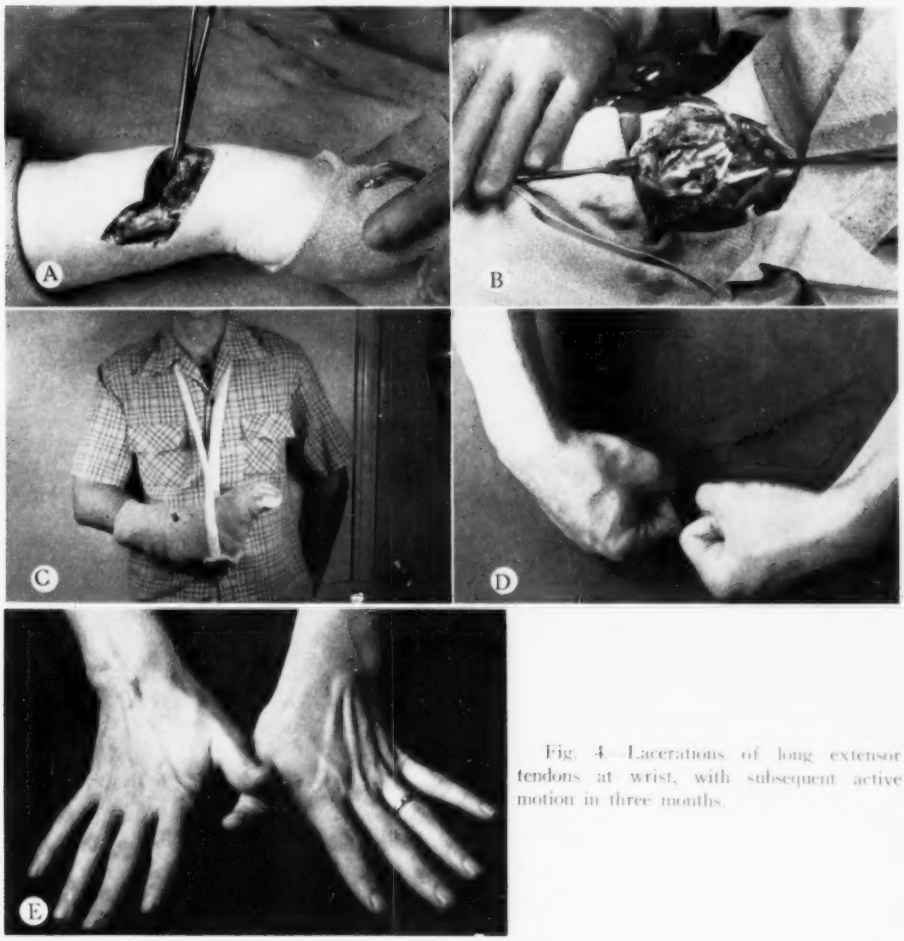


Fig. 4.—Lacerations of long extensor tendons at wrist, with subsequent active motion in three months.

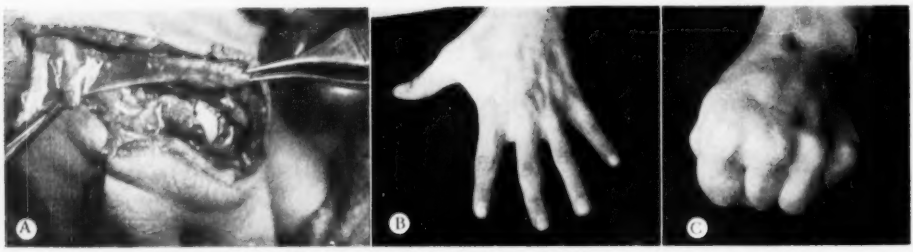


Fig. 5.—Laceration of long extensor tendons, extending into metacarpophalangeal joint spaces.

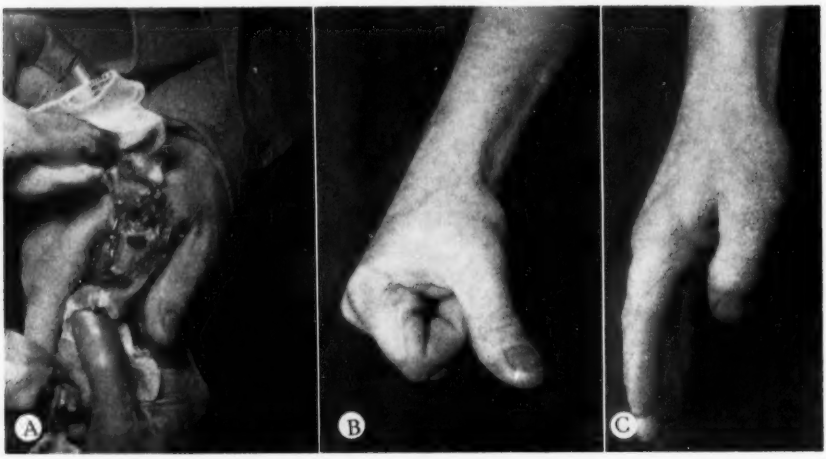


Fig. 6.—Avulsion of extensor aponeurosis and of middle slip of extensor indicis communis tendon, including periosteum and loss of bone from proximal phalanx and from head of metacarpal. Activity in six months.

and the hand splinted in extension, as in *C*. It may be noted that the interphalangeal joints are partially flexed on the splint, because they are not affected by the long extensor tendons. Only the wrist is extended to avoid any tension upon the sutures. *D* reveals full flexion in three months; *E*, free extension.

In Figure 5*A* the long extensor tendons to the index and middle fingers are cut through, as are the joint capsules, exposing the heads of the metacarpals. *B* shows free extension in five months, with some adherence of the skin to the anastomoses, which does not retard motion. *C* shows complete flexion.

In Figure 6*A* a power-saw cut has raised a flap from the dorsum of the proximal interphalangeal joint up to the metacarpophalangeal joint. It has avulsed and abraded most of the dorsal hood, as well as the central slip of the extensor indicis communis tendon. It has elevated and traumatized the periosteum. It has removed the dorsal base of the proximal phalanx and cut a wedge out of the head of the second metacarpal. Both pieces of bone were lost. Such a wound might be expected to leave extensive scarring in its wake.

The wound was gently cleansed with the usual white soap and water and all tissues carefully approximated with silk sutures on fine-eyed needles. The long extensor tendon was united with tiny 000000 silk sutures to the periosteum of the proximal phalanx; the edges of the periosteum were sutured, and all parts of the extensor mechanism were closed similarly. The hand was splinted in extension for three and one-half weeks. *B* shows nearly complete flexion in four months; *C* shows complete extension.

Comment

It seems wise, in the light of work that has been done upon tendon regeneration,[2] to keep the entire hand splinted for three and one-half weeks. After this period, I instruct the patient to carry his hand in

the sling for another week. He reapplies his splint lightly at night in order that he will not roll on the hand or strike the bed with it during sleep. He is warned not to pay heed to "friendly" advice of lay persons and not to apply any passive motion. During the week in the sling he inevitably moves the hand a little. He is cautioned to remove it from the sling several times a day in order to extend the elbow and move the humerus. He is told to take it out of the sling several times a day to wash both hands together, and even to leave it out of the sling when he is reading or watching T. V.!

By week's end, he is ready to keep the hand out of the sling and to stop splinting it at night. He is urged to use the hand for simple movements which help the other hand, such as buttoning clothes, tucking in shirts, combing his hair, and even feeding himself. He returns weekly to my office, and he is advised to assume more tasks as he seems ready.

There is still a great problem with the aged in body. If patients are kept with the hand in hyperflexion or hyperextension for three and one-half weeks, they may never straighten their wrist or use even their normal fingers again. Yet, because their healing is slow, if they are allowed full motion in less time, they may rupture the injured tendon. My own answer to this problem is to release them from their splints in two and one-half weeks and trust that the stiffness already present will prevent the amount of motion necessary to rupture the anastomosis, whereas the slight early motion may help prevent the severe stiffness (shortened joint capsules, volar plates, and collateral ligaments) that attends more prolonged immobilization.

Summary

Immediate suture of tendons following present-day rules of nontraumatic handling of tissues with adequate splinting for at least three and one-half to four and one-half weeks usually results in a good functioning hand. Those of little faith in nature, who may be tempted to advise early motion, may be rewarded with stiff fingers.

508 E. South Temple.

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Indications and Results in the Surgical Treatment of Pectus Excavatum

CONRAD R. LAM, M.D., and GEOFFREY L. BRINKMAN, M.D., Detroit

Pectus excavatum, or funnel chest, is a deformity characterized by depression of the lower sternum and adjacent costal cartilages. The lowest point is at the junction of the xiphoid process and the body of the sternum. It is commonly detected in early infancy, when it is noted that there is paradoxical retraction of the area on inspiration. During the next year or two, the costal cartilages and sternum become fixed, so that the depression is present regardless of the phase of respiration. The early problems are cosmetic and psychological (with effects on both the patient and his parents), but later there is almost inevitably some functional impairment. We have operated on 25 patients with pectus excavatum and are convinced that surgical treatment is remarkably effective and safe. This communication is presented with the hope that more young patients will receive specific corrective measures before anatomic changes have become relatively irreversible and before long periods of unnecessary psychic trauma have been endured.

Despite many hypotheses, the etiology of pectus excavatum is still obscure. Many of these theories are discussed in a review article by Ochsner and De Bakey,[1] published in 1939. Brown[2] and others have insisted that a short central tendon of the diaphragm is responsible, while Brodkin[3] and Chin[4] have postulated that muscular imbalance is the factor. Thus, there is general agreement that it is the diaphragm which in some way produces the mischief. The only basic etiologic factor of any importance is that of heredity. Relatives of 10 of our 25 patients also had varying degrees of pectus excavatum. Only 3 of the 25 were female, although this does not necessarily mean that there is that much difference in the incidence, since surgical correction is probably more in demand for males because of habits of dress on the beach, in summer camps, and the like.

Five children were operated on before the age of 2 years; six, between 2 and 5 years, and seven, between 5 and 15; four patients were between 15 and 25, and three were older than 25. The three female patients were in the older age groups, being 21, 29, and 37. Two of these were operated upon because of severe cardiac symptoms, and the other for psychological reasons.

The operative procedure for pectus excavatum has become more or less standardized. Most surgeons use some modification of the operation illustrated in Figure 17 in the article by Ochsner and De Bakey,[1] which represented the method previously used by Sauerbruch, Garnier, Matthieu, Truesdale, and Ochsner and De Bakey. Brown,[2] Lester,[5] Ravitch,[6] and Lindskog and Felton[7] have made contributions to the technique.

The essential features of the operation are indicated in Figure 1. The body of the sternum is separated from the xiphoid, and the deformed portions of the lower four or five cartilages are resected, leaving as much perichondrium as possible. A wedge osteotomy is made on the sternum by removing the outer table for several millimeters in a transverse direction to permit outward angulation. The sternum is main-

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Read before the Section on Pediatrics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

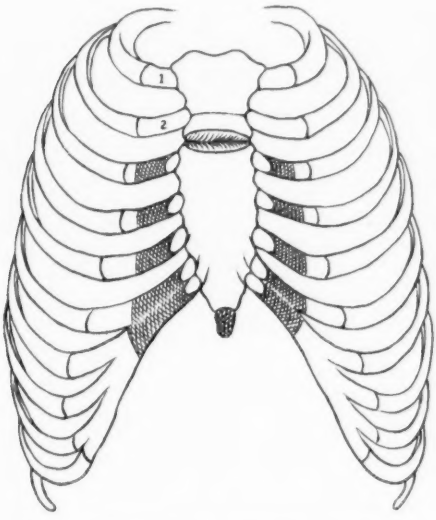


Fig. 1.—Diagram of operative procedure to correct the deformity of pectus excavatum. The cross-hatched portions of the costal cartilages are resected, and the direction of the sternum is changed by the wedge osteotomy at the second interspace.

tained in the corrected position by sutures placed through the periosteum of the sternum. Ravitch [6] has shown that external fixation with wires and bands passed around the sternum is usually unnecessary, and may be dangerous by providing a route for infection to enter a vulnerable wound. A rib strut to hold out the sternum was used only twice in our series, in cases of long-standing deformities in adults (Case 2).

We have been impressed with the cosmetic advantages of the transverse incision rather than a longitudinal one. The skin over the sternum is prone to keloid formation. In girls, this cosmetic detail is important in view of the changing styles in necklines, and it is worthy of consideration in boys as well. Certainly, the osseous and cartilaginous structures are just as easily exposed through the transverse incision.

There has been no operative mortality in the 25 operations in our series and no important morbidity. On rare occasions when the pleura has been opened, an intercostal drainage tube has been left in place for two days. Aspiration of serum which has collected subcutaneously has been necessary in a few patients.

The optimum age period for many children will be between 2 and 5 years. Infants under the age of 2 years cannot cooperate during the postoperative period, and nothing will be lost by waiting a few months. There is the remote possibility that the lesion will not progress or may disappear in early infancy.

The typical good result to be expected after early operation is illustrated in the photographs of Patient 1 (Fig. 2). He was first seen by us at the age of 5 years. In-

Fig. 2.—*A*, typical pectus excavatum deformity in a 5-year old-boy. *B*, immediate postoperative result; *C*, result two years later.

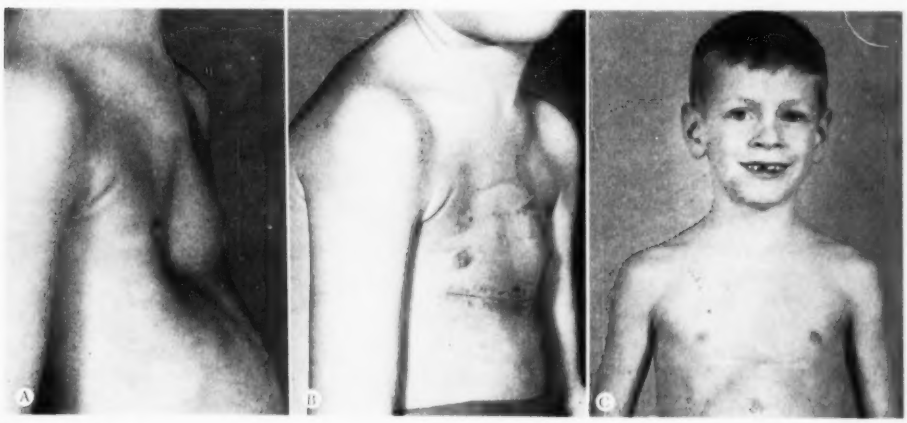
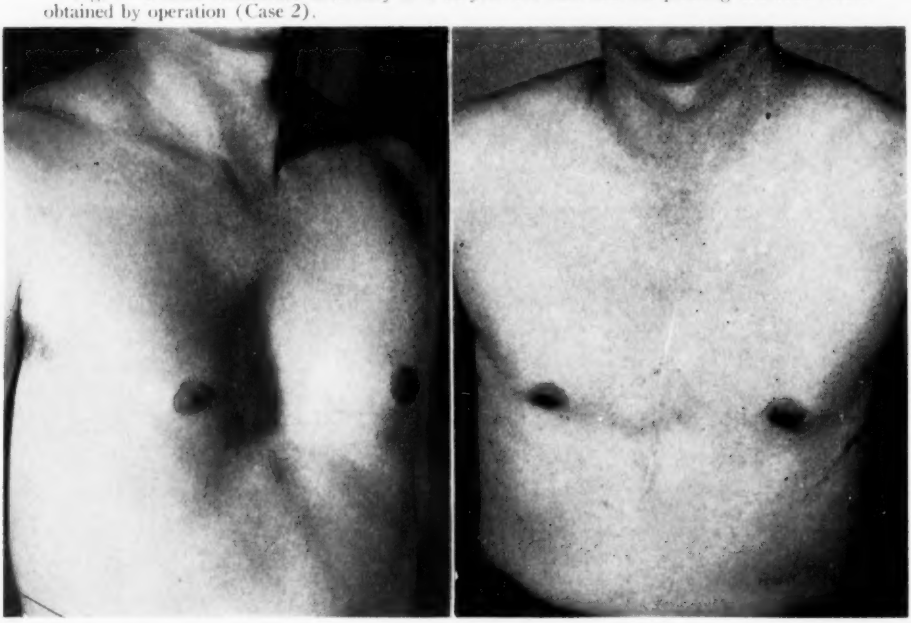


Fig. 3.—Cartilages resected in Case 1.

Fig. 4.—Pectus excavatum deformity in a 30-year-old man and the pleasing cosmetic result obtained by operation (Case 2).



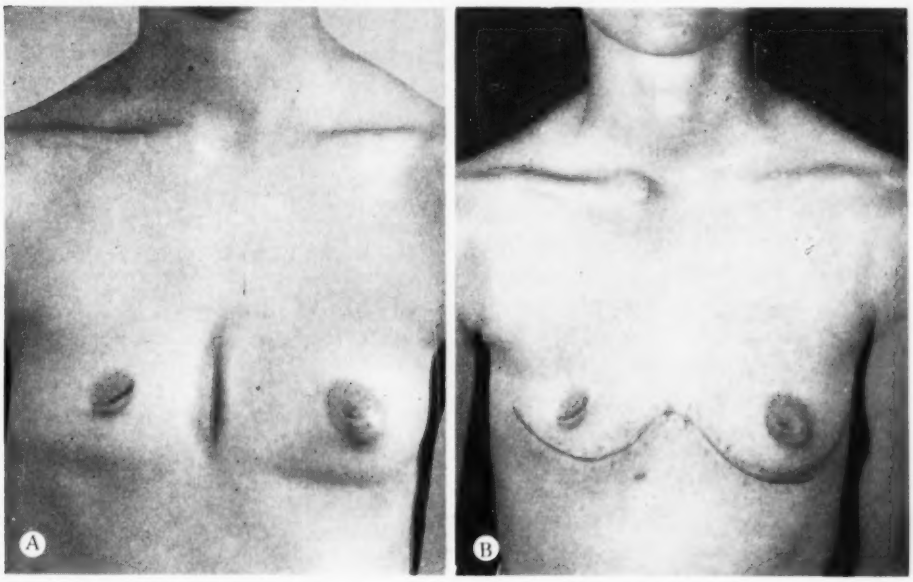
spiratory retraction of the lower sternal region had been noted soon after birth. The deformity had gradually become more pronounced. Operation was recommended to the parents, and they gave their consent. The typical operation through a transverse incision was carried out. Follow-up observation two years later showed a near-perfect cosmetic result.

Case 2 is an example of the importance of psychological factors in pectus excavatum. This man was first seen at the age of 30. He had had a pectus deformity since infancy, and throughout his life he had been antisocial because he was so self-conscious of his chest deformity. He never went swimming or took part in athletic activities. For the same reason, he shunned any association with the opposite sex and lived the life of a social recluse. He was eventually drafted into the Army, but was discharged because of a systolic heart murmur. Operative correction was advised and was carried out by Dr. Leo Kenney, with gratifying results (Fig. 4*B*). After the operation his life was completely altered. He has become a very sociable and dynamic person and is now a successful salesman. Furthermore, he then felt able to go swimming in public, and before long he wooed and won himself a wife and now is the father of two children. This case is an example of the psychic trauma which persons with the deformity may suffer, and this consideration alone justifies the operation in the vast majority of patients.

In the severer degrees of the deformity, the anteroposterior diameter of the chest is so narrowed that the heart is displaced to the left and may undergo some degree of compression. Dyspnea on effort is common at an early age. The condition may progress to severe exercise intolerance, with palpitation, sweating, precordial pain, and fainting. Cardiac catheterization has shown that there may be elevation of the right auricular and right ventricular pressures, and that with exercise no increase in cardiac output is possible.

Operation was recently carried out on a 21-year-old woman for severe cardiac symptoms (Case 3, Fig. 5). Pectus excavatum deformity had been noted at birth. By the age of 5 years her exercise tolerance

Fig. 5.—*A*, pectus excavatum deformity in a 20-year-old woman (Case 3) with symptoms of compression of the heart; *B*, postoperative result two months after operation.



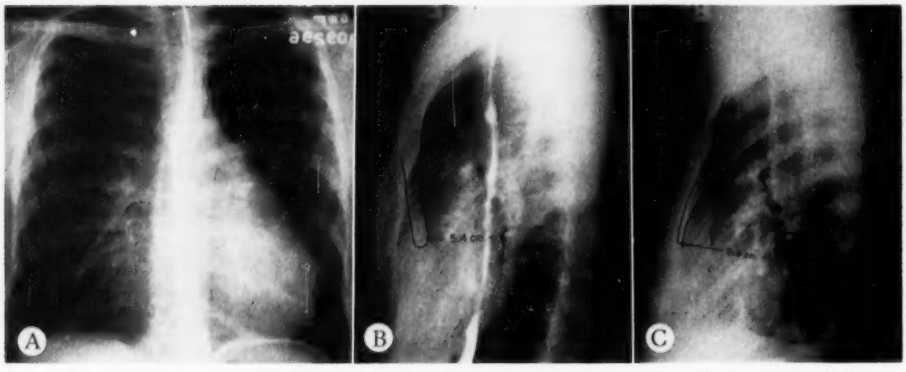


Fig. 6.—Roentgenograms in Case 3. *A*, posteroanterior view, showing displacement of the heart to the left; *B*, preoperative lateral film, showing sternal displacement; *C*, postoperative film, showing correction of sternal compression of heart.

was so limited that she could not take part in normal childhood activities. She married at the age of 16 and had two children, but by the age of 20 the dyspnea had become so severe that she could not take care of her household duties and the children. She was then unable to go up a flight of stairs, and even a moderate amount of exertion brought on precordial pain, palpitation, and fainting. On physical examination, it was noted that she had a well-marked pectus excavatum deformity. There was a systolic murmur over the pulmonic area. The posteroanterior roentgenogram of the chest showed displacement of the heart toward the left, and the lateral film indicated that the distance between the depressed sternum and the vertebral column was only 5.4 cm. (Fig. 6). Operation was carried out and a satisfactory cosmetic result was obtained. The postoperative lateral roentgenogram of the chest showed that the distance between the sternum and the vertebral column had been increased to 8.4 cm. Her cardiac symptoms have disappeared.

A follow-up study of the 25 patients has shown that 21 of them have results which can be classified as excellent. The other four have at least 50% correction of the deformity. Three of these "fair" results were in older patients.

Summary

The etiology of the malformation of the thoracic cage commonly known as pectus excavatum, or funnel chest, is poorly understood, but the clinical course of the child in whom it is observed in infancy can be predicted with considerable certainty. The deformity will persist and become more noticeable as time passes. The difficulty is chiefly a cosmetic one, although in severe cases there may be disturbance of respiratory and cardiac function. Surgical correction at an early age is feasible and advisable from the standpoint of the psychological effect on the child and his parents. The operation consists of resection of the deformed cartilages and a wedge osteotomy of the sternum. Twenty-five patients have been operated on, with gratifying results.

Henry Ford Hospital (2).

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Influence of Route of Administration on Effectiveness of Clostridial Antitoxin

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In his masterful and comprehensive review of the biology of anaerobic infections, Prévot [1] gives limited space to the antitoxin therapy of gas gangrene due to Clostridium perfringens. Essentially, he covers the entire subject with the statement: *Contre la toxine circulante, seule la sérotherapie est efficace.* Logically, this should cover the matter. However, surgeons with extensive knowledge of clinical gas gangrene are increasingly tending to deemphasize the role of antitoxin in clinical use, or have abandoned it altogether. The United States Army has recently dropped gas gangrene antitoxin from its standard stock list. The recommendations of the American College of Surgeons on the use of antitoxin are couched in cautious terms.[2]

Actually, there is relatively little independent proof of the existence in gas gangrene of a true "toxemia," and there is certainly considerable doubt extant on the question of whether there is a "circulating toxin." On the basis of the difficulties in detecting toxin in the blood stream, even after the intravenous injection of large doses, MacLennan and Macfarlane [3,4] have hypothesized that the actual site of action of the toxin is in the local area of infection, and that systemic effects are due to secondary products. These products may not be neutralized by antitoxin, which is produced by using an antigen developed from filtrates of in vitro cultures.

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In addition to the possibility that the standard antitoxin may not be effective against the true circulating toxin, whatever it is, in our opinion the clinical disappointment in the efficacy of clostridial antitoxin may be simply a question of too little and too late. As to its use too late, this is virtually inherent in clinical treatment. Evans [5] has shown that it takes only about one-hundredth as much antitoxin to protect an animal against experimental infection if the antitoxin is administered *before* the animal is infected, in comparison with administration of antitoxin six hours after the organisms are injected. As to the question of too little, we have little more than our own impression. By analogy with the unit dosage used clinically in other toxigenic diseases (diphtheria and tetanus), and the relatively small mass of tissue which may be involved in these diseases in comparison with gas gangrene in large muscle groups, the customary dosage of gas gangrene antitoxin would appear to be minimal. In a limited number of preliminary experiments (not elsewhere reported) we have found that a dose of C. perfringens antitoxin of 4,000 units per kilogram, given intravenously two to three hours before wounding, is of quite limited effectiveness in prolonging the survival time of goats and guinea pigs with C. perfringens infection in a massive experimental wound.

We have been unable to obtain a supply of high-concentration antitoxin in quantities sufficient to permit experimentation with such large doses in a large series of goats, and we do not feel that our comparable guinea pig preparation is sufficiently well

standardized as yet to support valid conclusions. Consequently, it has appeared indicated to us to determine whether the administration of antitoxin directly into the infected area might influence the effectiveness of a given (marginal) dose of antitoxin. Local administration could conceivably be more effective, either by blocking the primary effect of toxin in breaking down tissue and producing secondary toxic products or by providing a tighter "main line of resistance" in keeping toxin from entering the blood stream.

Materials and Methods

Our preparation is a massive bilateral open wound in the hindquarters of the goat, standardized by Ochsner et al.[6] for the study of traumatic shock. The goats are all Texas Angora wethers (castrated males) 5 to 8 years old and weighing 35-50 kg. The wounds are produced by the detonation of high-explosive pellets placed over the lower third of the thighs. Untreated, the preparation is uniformly lethal in approximately 20 hours. Recent studies[7-9] have confirmed the long-standing suspicion that the natural course of the preparation invariably includes a severe infection of the wound with C. perfringens.

The antitoxin utilized was standard U. S. Navy stock, procured by the Government from commercial sources: Gas-Gangrene Antitoxin (Trivalent), Type 2. Per vial, it contained 9,000 units of C. perfringens antitoxin, 9,000 units of C. novyi antitoxin, and 4,500 units of C. septicum antitoxin. Each vial delivered approximately 12 ml. of solution containing 17.0 gm. % of globulin.

The control serum utilized was prepared by the same manufacturer from slaughterhouse horse serum.* It showed an exactly comparable paper-electrophoretic curve but assayed at a slightly lower protein content: 15.4 gm. %.

Animals (except untreated controls) were injected with the content of 10 vials of antitoxin, or 130 ml. of processed serum, two to three hours before wounding. Of the treated animals, half were given the antitoxin or serum dose intravenously. The other half were given the dose by infiltration into the muscles of the hindquarters, including the gluteus, quadriceps, and hamstring muscle groups. For both intravenous and local administration, the dose of serum or antitoxin was diluted with isotonic saline to a total quantity of 1 liter.

TABLE 1.—*Effect of Clostridial Antitoxin and Processed Horse Serum in Prolonging Survival Time in Wounded Goats*

		Serum		Antitoxin	
Treatment	None	I. V.	Local	I. V.	Local
N *	100	18	18	24	24
M. S. T. †	21.32	20.08	21.98	22.57	25.67
S. E. M. ‡	±0.78	±1.47	±0.85	±1.90	±1.73

* N = number of animals in group.
† M. S. T. = mean survival time in hours.
‡ S. E. M. = standard error of mean survival time.

TABLE 2.—*Analysis of Variance: Effect of Antitoxin and Route of Administration* *

Variance Source	*d. f.*	*SS*	*MS*	*F*	*P*
Between Groups					
A BC *vs.* DE	1	294	294	4.98	<0.05
D *vs.* E	1	117	117	1.98	>0.05
A *vs.* BC	1	2	2	†	†
B *vs.* C	1	32	32	†	†
Within groups (Error)	179	10,564	59		
Total	183	11,009			

* *d. f.* = degrees of freedom; *SS*, sums of squares; *MS*, mean square; *F*, variance ratio; *P*, probability expression of statistical significance; A, no treatment; B, serum, i. v.; C, serum, local; D, antitoxin, i.v.; E, antitoxin, local.
† Variance within groups is greater than variance between the groups compared.

Results

Results are summarized in Tables 1, 2, and 3.

The survival time of animals in the control (untreated) group was entirely consistent with the survival time of recent series of untreated animals studied in these laboratories and with the cumulative control data on this preparation.

Animals treated intravenously with processed serum showed a statistically negligible decrease in mean survival as compared with untreated animals.

Animals treated by local infiltration of processed serum showed a minimal, and statistically insignificant, increase in survival time.

* The Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y. furnished this serum.

TABLE 3.—*Effect of Route of Administration of Antitoxin*

	Control Series	
	A_I	A_{II}
	50	50
M. S. T.	21.36	21.27
S. E. M.	0.99	1.21

Local antitoxin *vs.* control series A_I: $t(72)=2.160$ $P<0.05$
Local antitoxin *vs.* control series A_{II}: $t(72)=2.080$ $P<0.05$
Intravenous antitoxin *vs.* control series A_I: $t(72)=0.564$ $P>0.5$
Intravenous antitoxin *vs.* control series A_{II}: $t(72)=0.576$ $P>0.5$

Animals treated with intravenous antitoxin showed a slight increase in survival time, but there was such variation within the group that the difference is not statistically significant.

Animals treated by local infiltration of antitoxin showed a slight increase in absolute survival time: a gain of less than five hours, an increase of *22%* in time of survival, as compared with untreated controls. However, the effect was sufficiently consistent to be of statistical significance ($P<0.05$).

Analysis of variance indicates that antitoxin treatment is significantly effective but does not demonstrate a superiority of local over intravenous administration. The total control series was divided into two series by alternate apportionment of untreated animals from the sequence in which they were wounded. Regardless of which of these two series of 50 animals is chosen as an "intravenous" control and which as a "local" control, local administration of antitoxin is demonstrated to be significantly effective; intravenous administration is *not* significantly effective.

Comment

The indications are that a given dose of antitoxin may be more effective by local infiltration than by intravenous administration. The data are insufficient to support even a rough tentative quantitation, such as "50% more effective" or "twice as effective." The apparent increase in effect is more remarkable in view of the fact that the animals lose one-fourth or more of the injected dose through the effect of blast at wounding and through early losses of tissue fluid through the wound. We have no data, and offer no conjecture, as to whether the enhanced effectiveness of locally infiltrated antitoxin is due to its immediate presence at the wound site, or due simply to being injected intramuscularly.

Conclusion

In a standardized experimental wound in the goat, which has been shown to harbor a severe clostridial infection, clostridial antitoxin administered by local intramuscular infiltration offers a significant protective effect, but the same dose of antitoxin administered intravenously has not been demonstrated to be effective.

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Carbon-Black Carcinoma of Stensen's Duct

Report of a Case

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Because of the critical anatomic position of the parotid duct, malignancy of this structure presents a serious cosmetic and surgical management problem both to the patient and to the physician. The paucity of experiences and therapeutic guides in the literature is attributable to the rarity of this disease entity, only six cases having been reported. No case of parotid duct malignancy in which carcinogenic constituents of carbon black are implicated has heretofore been reported.

Goforth [1] reported an anaplastic epidermoid carcinoma in the parotid duct of a 60-year-old woman. The tumor was excised, along with a small segment of the duct and a small amount of cheek tissue. The excisional site was treated with radium. A single cervical lymph node revealed metastatic cancer. A radical neck lymph node dissection was not performed. The patient died of widespread tumor metastases one and one-half years later.

Figi and Roland [2] reported an adenocarcinoma that had developed in the parotid duct of a 62-year-old man. No cervical nodes were felt. The tumor was excised with a small margin of cheek tissue, and the proximal end of the parotid duct was fistulized to the buccal cavity. No radical neck lymph node dissection was done. The excisional site was treated with radium. A three-year follow-up reported the patient to be well and apparently free of tumor. These authors reported a second adenocarcinoma of the parotid duct in a 55-year-old physician. This was treated with local excision and radium. No radical neck lymph node dissection was done. An eight-year follow-up reported that the patient was well and apparently free of tumor.

Smith, Gratiot, and Simard [3] reported a sarcoma of the parotid duct in a 29-year-old man. This was initially treated by local excision. One month later, they performed a radical excision of the skin and soft tissues of the face, including the parotid gland. Five months later, a radical neck lymph node dissection was performed. Many cervical nodes contained tumor. The patient died of widespread tumor in the spine and viscera one year following the initial surgical procedure.

Beyer, Blair, and Hamilton [4] reported a papillary adenocarcinoma of the parotid duct in a middle-aged man. The lesion was locally excised and treated with radium. One year later a suprahyoid lymph node dissection was done. The nodes did not contain cancer. A 20-year follow-up reported the patient to be well and free of cancer. These same authors reported a papillary adenocarcinoma in the parotid duct of a 58-year-old woman, which was treated with local excision. The neoplastic cells were found in the perineural lymphatics. The parotid was not excised; radium was not used, and no radical neck lymph node dissection was performed. No follow-up is reported.

Carbon black is amorphous carbon with a particle size ranging from about 10μ to about 200μ. Carbon black is a form of soot, and sometimes the two terms are loosely used to designate identical or related products. Soot is an all-inclusive term applied to amorphous carbon produced

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by the combustion of most organic substances, and has a particle size of 10μ to 5,000μ. All of us are exposed to varying amounts of soot. In its simplest form, carbon black can be produced by holding a cold plate in the flame of a Bunsen burner that is burning ordinary city gas. The resulting black deposit on the cold plate is carbon black. Carbon black is widely used in industry in the manufacture of tires, paints, dyes, etc. Each of these applications requires a particular type of carbon black. At a temperature range of 1,100 to 1,600 C, which is that used to produce carbon blacks, all known hydrocarbons tend to decompose into amorphous carbon and hydrogen gas.[5] The size and quality of the particle and its physicochemical nature can be altered by many factors, which include temperature and time of reaction, type and chemical composition of the hydrocarbon burned (i. e., methane *vs.* propane *vs.* butane *vs.* tar and gasoline), and the type of atmosphere employed for combustion. In the manufacture of furnace carbon blacks, the pyrolysis of gases produces complex aromatic polycyclic hydrocarbons,[6,9,11,12] which may be considered contaminants of the pure amorphous carbon. These hydrocarbons are benzene and acetone-extractable. Steiner has identified 3,4-benzpyrene, 1,2-benzpyrene, pyrene, fluoranthene, 1,12-benzpyrene, anthanthrene, and coronene. Furnace carbon blacks, with an average particle size of 80μ or larger, contained all seven of the above hydrocarbons. However, most of those with a particle size below 50μ had fewer polycyclic hydrocarbons on benzene extraction.

Steiner[7,8] produced epithelial and connective tissue malignant tumors in the salivary glands of rats, mice, guinea pigs, and rabbits (Tables 1 and 2). He embedded these aromatic polycyclic compounds in pellets and placed them surgically in the salivary gland of the experimental animals (Tables 1 and 2). The most obvious offender was 3,4-benzpyrene. He also demonstrated the presence of these polycyclic compounds in the rubber of tires and found that they were a contaminant of the particular carbon black employed in rubber.[12] Carbon black is used to reinforce and strengthen the rubber employed in the manufacture of tires, and is not used primarily to color the tire. As much as half the weight of the rubber employed in the tire may be due to the carbon black. He postulated that carbon black, under certain cir-

TABLE 1.—*Summary of Experiments in Which Epithelial Metaplasia and Tumors Were Observed* *

Experiment	Species	Chemical	Tumors of Given Type Produced										
			No Epithelial Change	Metaplasia to Squamous Cell	Epidermoid Cyst	Sarcoma	Hemangiosarcoma	Adenocarcinosarcoma	Acanthocarcinosarcoma	Acanthoadenocarcinoma	Adenocarcinoma	Squamous Cell Carcinoma	Total
1	Mouse	Methylcholanthrene	8	16	..	13	3	2	2	1	1	2	47 †
2	Mouse	1,2,5,6-dibenzanthracene	6	4	1	..	..	..	..	1	..	8	20
3	Mouse	Cholesterol	21	..	..	..	..	..	..	..	..	..	21
4	Rat	3,4-benzpyrene	3	..	..	2	..	1	..	..	..	3	9
5	Rat	Methylcholanthrene	2	8	1	1	..	..	..	..	..	4	16
6	Guinea pig	Methylcholanthrene	10	4	7	1	..	..	..	..	..	3	25
7	Guinea pig	Cholesterol	3	..	..	..	..	..	..	..	..	..	3
8	Rabbit	Methylcholanthrene	6	4	1	..	..	..	..	..	..	..	11

* The wide variety of tumors that developed in the salivary glands of mice, rats, guinea pigs, and rabbits following the local implantation of carcinogenic chemicals is strikingly recorded in this Table, reproduced from Steiner's study,[8] with permission of the author.

† One mouse had two tumors.

TABLE 2.—*Summary of Experiments in Which Carcinomatous Changes Were Induced* *

Experiment	Species	Chemical	Amount of Chemical, Mg.	Induction Time for First Tumor, Mo.	Effective Total of Animals	Tumors	Percentage Yield of Tumors	Average Induction Time, Mo.
1	Mouse	Methylcholanthrene	1	3.75	11	8	72.7	10.25
2	Mouse	1,2,5,6-dibenzanthracene	1	4	15	10	66.6	8.2
3	Mouse	Cholesterol	2.5	--	--	0		
4	Rat	3,4,-benzpyrene	3	13	6	3	50.0	15.3
5	Rat	Methylcholanthrene	5	7	6	5	83.3	9.5
6	Guinea pig	Methylcholanthrene	10	11	5	3	60.0	24.75
7	Guinea pig	Cholesterol	20	--	--	0		
8	Rabbit	Methylcholanthrene	10	--	--	0		

*Table 2 reproduced from Steiner's study with permission of the author.

cumstances,[12,13] would eventually be found to produce cancer in man.

We present this unusual and difficult case to outline our therapy, and to report what we believe to be clinical substantiation of Steiner's prediction, i. e., that carbon black can produce clinical cancer in man.

Report of Case

A., a 53-year-old white man, was admitted to the New York Hospital on April 5, 1956, because of a painful nodule in the soft tissues of the right cheek.

For a number of years the patient had noticed intermittent puffiness of both cheeks, alternating between the right and the left side, and at this time there was some swelling of the lids of the eyes. Two weeks prior to admission Mr. A. had developed a swelling of the right cheek extending to the ear, and he thought he had "mumps." Gradually the swelling disappeared, and he became aware of a hard nodule in the soft tissues of the right cheek opposite the upper back molars. His family physician believed this to be a stone in Stensen's duct.

Mr. A. was a research chemist who experimented in the production of many types of carbon black. During the period of his employment, from 1941 to 1952, he had handled most commercial carbon blacks and more than 170 different experimental carbon blacks, made in his own carbon-black furnace. The exposure was particularly heavy between 1945 and 1948. Most of his experimental carbon blacks were produced from a mixture of city gas and Pyrofax. The patient stated that the acetone-extractables of his experimental carbon blacks varied from 0.5% to 5.0%. He was exposed to commercial carbon blacks having a mean particle diameter of from 35μ to 270μ. His experimental carbon blacks varied from 50μ to 100μ in particle diameter. The patient produced many of his experimental furnace blacks in the pH range of 2.4 to 8.6. He was exposed to commercial carbon blacks produced at a pH of 3.6 to 10.4.

In 1952 the patient felt in poor health and generally unable to continue his occupation, as the result of a constant feeling of fatigue. He was not employed from 1952 to 1956, but was supported by his wife. Prior to this present illness, the patient had always been well. There is no family history of cancer.

Physical examination disclosed a well-developed, moderately obese, tense, pale white man. The temperature, pulse, and respirations were normal, as were the heart, lungs, and abdomen. The blood pressure was 123/90. The buccal orifice of the right parotid duct was puckered. A firm, 0.5 cm. nodule was palpable in the soft tissue of the cheek 1 cm. posterior to the orifice of Stensen's duct. No cervical lymph nodes were felt.

The urine was normal. Hemoglobin was 17.4 gm. %; red blood cells numbered 5,000,000, and the white cell count and smear were normal. The chest x-ray was normal.

On April 12, 1956, the nodule in the right cheek was incised, and, since no stone was encountered, a segment of tissue was removed for frozen section. This revealed an epidermoid carcinoma Grade 2 or 3 (Fig. 1). Because of this unexpected finding, the entire mass was removed, including muscle, fat, and the orifice of the parotid duct. The duct, as it emerged from the parotid gland proximal to the excised segment, was fistulized to the buccal cavity.

Careful evaluation of the literature failed to suggest a course of therapy. The x-ray therapy consultant did not feel that radium would contribute to the treatment in this case. Recommendations of surgical consultants varied from conservative local excision to radical excision of the duct, gland, neck nodes, and mucosa of the mouth, including the maxillary sinus on the right side. As a compromise, on April 12, we performed a radical excision of the parotid gland and Sten-

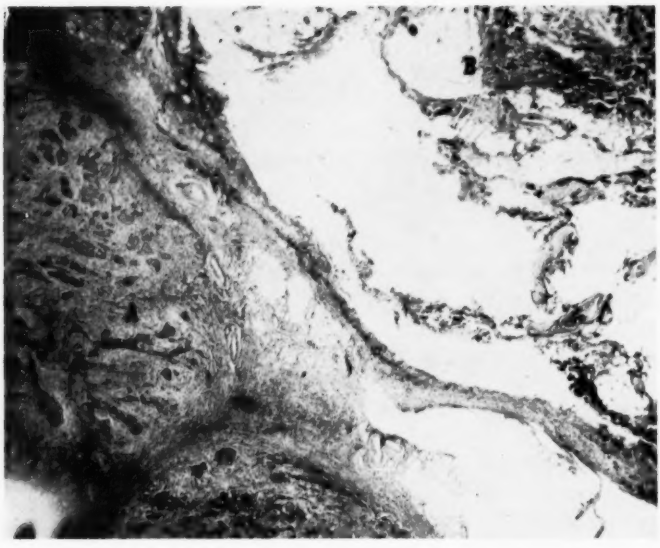

Fig. 1.—Stensen's duct. The site of the nodule (*A*) is filled with and replaced by epidermoid carcinoma, Grade 2 or 3. The entire mass was removed with cheek tissue, including muscle (*B*) and fat.

sen's duct and all cheek tissue along the duct, including skin. A suprahyoid lymph node dissection was carried out.

Persistent carcinoma was found in the cheek tissue around the former site of excision. The lymph nodes did not contain cancer. The remaining segment of Stensen's duct was lined with stratified squamous epithelium and was considered normal. The parotid gland was free of cancer. Most of the glandular elements had disappeared and were replaced by fat infiltrated with groups of lymphocytes. The duct system of the gland was dilated. The lower branch of the right seventh nerve was included in the specimen.

Three months after discharge, the patient developed left parotitis, which responded slowly to antibiotics. At this time, induration was noted in the scar of the right cheek, and a hard nodule was noted in the right posterior cervical triangle. Mr. A. entered the New York Hospital for the second time, on Sept. 30, 1956. A local excision of the soft tissues of the right cheek was carried out, and radical neck lymph node dissection was performed. Recurrent cancer was found in the cheek tissue and in two lymph nodes (Fig. 2) in the posterior cervical chain. He was discharged from the hospital on Oct. 25, 1956.

Because the buccal mucosa wound never completely healed and the patient noted a painful nodular crater surrounding a 3 mm. ulcer, he was admitted for the third time, on Jan. 7, 1957. A radical excision of right maxillary bone and soft palate and excision of soft tissues of the cheek were performed. He made an uneventful recovery following this procedure. A split-thickness graft was taken from the left thigh and placed to line the right cheek, extending from the ramus of the mandible to the base of the orbit of the eye. The patient was discharged from the hospital on Jan. 27, 1957.

Intermittently during the year 1957, he developed subacute and acute parotitis, which responded to antibiotics. A sialogram disclosed marked ectasia of the left parotid duct system. Because of recurrent bouts of difficulty associated with the left parotid gland, the patient was admitted to the New York Hospital for the fourth time on March 1, 1958, and the left parotid was removed. This showed marked dilation of the duct system and squamous-cell metaplasia. At operation the gland was exceedingly difficult to dissect out because of many adhesions and because of its vascularity and extensions around and under the ramus and angle of the mandible. As the orbital branch of the seventh nerve was dissected out of the gland, a great deal of black material was found on the wiping sponges. Histologic study of the gland disclosed a black material in the gland and lymphocytes and multinucleated giant cells (Fig. 3). The patient was discharged on March 23, 1958. The cosmetic result following this extensive surgery is good (Fig. 4). The patient's right cheek was lined with a split-thickness skin graft. The soft tissues of the right cheek are maintained in normal position by an acrylic dental prosthesis. Phonation is poor unless the prosthesis is employed, and then it is good. The patient, when examined on Dec. 4, 1958, felt and appeared quite well.

Comment

The literature reports only one previous case of epidermoid carcinoma of the parotid

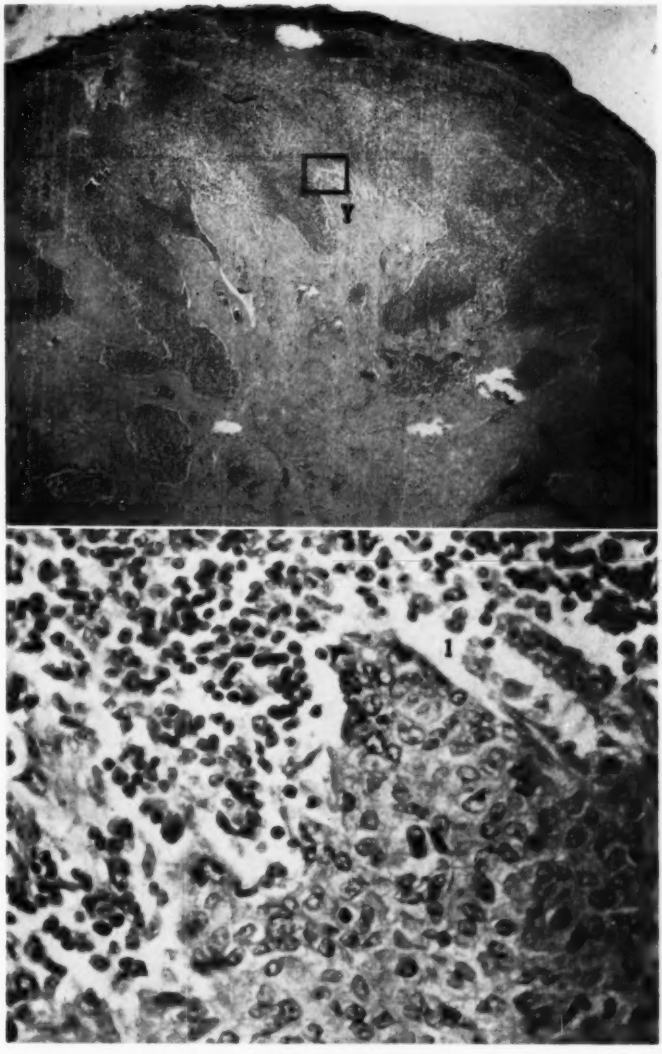

Fig. 2.—(*A*) Above: Low-power study of the lymph nodes from the right posterior cervical chain revealed almost complete replacement with cancer ×40. Below: Higher magnification of a randomly selected area (*Y*) disclosed carcinoma Grades 2 and 3, with mitosis, as indicated by *1* ×140.

duct. This was treated by local excision and radium, which did not effect a cure. Four cases of adenocarcinoma of the parotid duct have been reported. Three of these were treated with local excision and radium, with reported survival of from 3 to 20 years. The fourth case was treated by local excision, but no follow-up is reported. All of these cases occurred in men and women in the sixth and seventh decades of life. The one reported case of sarcoma of Stensen's duct occurred in a 29-year-old man. It was treated by radical excision of Stensen's duct, the parotid gland, and the cheek tissues, and this was followed by a radical neck lymph node dissection, with death following within a year.

From the reported experience, one might be tempted to treat an adenocarcinoma of the parotid duct by local excision and follow this with radium treatment. Apparently, there is a difference in cell-type characteristics between adenocarcinoma and epidermoid carcinoma of Stensen's duct, for the

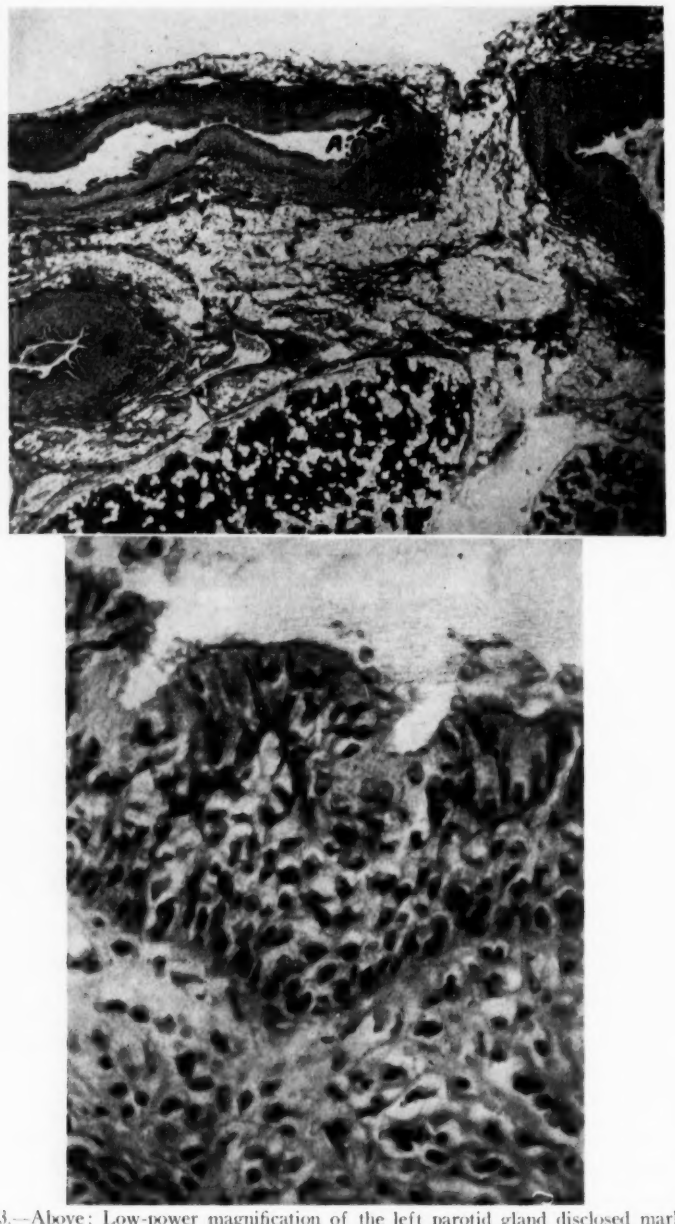

Fig. 3.—Above: Low-power magnification of the left parotid gland disclosed marked dilatation of the duct system. Many ducts (*B*) contained an amorphous black material. Squamous metaplasia with papillary change was apparent everywhere in the parotid gland duct system (*C*). Below: Higher magnification from *A* disclosed the marked squamous metaplasia × 180.

one patient with epidermoid carcinoma of the parotid duct treated with local excision and radium died within one year, whereas at least three of the four reported patients with adenocarcinoma survived. Our x-ray therapy consultants felt strongly that radium and other forms of radioactive therapy would not afford adequate protection in this

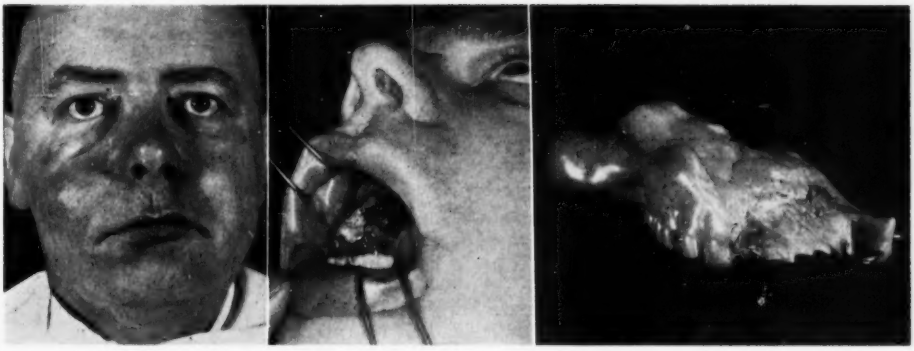

Fig. 4.—The cosmetic result following this extensive surgery is good. The patient's right cheek is lined with a split-thickness skin graft obtained from the left thigh. The right cheek tissues are maintained in normal position by an acrylic dental prosthesis, bearing teeth, to replace the excised maxillary bone and soft tissues. Phonation is poor unless the prosthesis is worn, and then it is fairly good.

case. One of us (B. M.) was originally of the opinion that adequate surgical excision must include excision of Stensen's duct, the parotid gland, and an adequate margin of cheek tissue about Stensen's duct, including muscles, skin, and buccal mucosa. He felt that this should be followed by a regional radical neck lymph node dissection. However, surgical consultants disagreed on the necessity for extensive surgery, and our therapeutic course was influenced by these consultants and by the patient's concern and our concern lest we do mutilating facial surgery. The clinical course of this case confirms our feeling that the management of epidermoid carcinoma of the parotid duct must include wide local excision, with adequate margin of cheek tissue in continuity with the parotid gland and wide excision of the buccal mucosa and skin of the face. To achieve a wide margin of the buccal mucosa, it is imperative that a cheek-tissue flap be turned back and that the maxillary sinus be removed, including hard and soft palates. This should be followed by a radical neck lymph node dissection. This course of treatment has now been completed, and the cosmetic result is quite good (Fig. 4). Our consulting dentist fitted Mr. A with an acrylic prosthesis that fills the defect under the right cheek and carries the right upper maxillary denture. This prosthesis has afforded the patient normal phonation. It has now been 20 months since the radical surgery, as noted above, was completed, and the patient shows no evidence of persistent or recurrent carcinoma.

Sweitzer and Heller [11] discussed many of the problems and much of the chemistry involved in the formation of carbon blacks in hydrocarbon flames. They suggested that benzene or acetone extracts of carbon blacks would vary from 0.2% to as much as 30% in contaminate components, including apparently these polycyclic compounds. Among the contaminants they found pyrene, fluoranthene, 3,4-benzpyrene, anthanthrene, 1,2-benzpyrene, benzperylene, and coronene. They suggested that there might be even more complex polycyclic structures on the carbon surface, such as rhodacene ($C_{30}H_{16}$) and leucacene ($C_{54}H_{32}$). The percentage of this extractable matter, they felt, could be held within minimal limits by control of temperatures and contact time. Benecke and Schröder [9] produced squamous-cell carcinoma in a mouse and sarcoma of the parotid gland in mice and rats with benzypyrene. Rusch, Baumann, and Maison [10] reported sarcoma and squamous-cell carcinoma of the submaxillary gland induced in mice with benzpyrene, and sarcoma induced in rats with dibenzanthracene. Steiner produced epidermoid malignant tumors and sarcomas in the salivary glands of mice, rats, guinea pigs, and rabbits, em-

ploying 3,4-benzpyrene. Steiner found lining-cell changes in the salivary gland ducts, varying from squamous metaplasia to neoplasia.

In his laboratory and in cleaning his own experimental furnace, Mr. A. was repeatedly exposed to atmospheres that contained a wide variety of carbon blacks. These were present often as a microscopically fine "soot" everywhere in his occupational environment. At times, he literally ate and breathed this material as it contaminated the air. The patient noted it as a gritty black material in his mouth, and frequently on sneezing he noticed it on his handkerchief.

At first glance, one is forced to consider how this carbon black material proceeded retrograde up Stensen's duct on the right side, and retrograde up Stensen's duct into the parotid gland on the left side. Clinically, all surgeons have learned that the peristaltic flow of saliva from the salivary glands to the buccal cavity is not necessarily unidirectional, for bacteria will ascend the parotid duct from the mouth to the parotid gland and produce "surgical parotitis." It is quite plausible, therefore, that fine particles in the order of 10μ to 20μ, or even larger particles of carbon black, could similarly proceed through Stensen's duct to the parotid gland.

Inasmuch as the polycyclic chemical contaminants of carbon black are known carcinogens in animals, and since the old, well-known observation of Percival Pott [14,15] on the carcinomas induced by soot on the skin is an established fact, it is plausible that the carbon black produced the parotid duct cancer in this case.

This conclusion is appreciably reinforced by the presence of squamous metaplasia, a probable precancerous lesion in the left parotid gland. In this parotid gland, a black material was noted in the gross specimen and in the histologic study. This foreign material had produced a foreign-body multinucleated giant-cell reaction. Glandular tissue, unfortunately, was not submitted for chemical analysis for the presence of polycyclic chemicals or of carbon black.

Summary and Conclusions

Six cases of malignant disease of the parotid duct reported in the literature are summarized and discussed.

A case of epidermoid carcinoma of the parotid duct and squamous metaplasia of the parotid gland is reported.

The relationship of the polycyclic contaminants of carbon black to malignant disease of Stensen's duct is reported in animal studies. The probable relationship of carbon black to cancer of the parotid duct and squamous metaplasia of the parotid gland in our case is discussed.

The radical surgical care of carcinoma of Stensen's duct should involve excision of the parotid duct with a margin of cheek tissue and a margin of skin and buccal mucosa in continuity with the parotid gland. This should be followed by a radical neck lymph node dissection.

The cosmetic result following radical surgical excision of cancer of the parotid duct is good.

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Our Changing Cardiovascular Attitudes Toward Major Surgery

Two Hundred Four Cases of Major Surgery Reviewed

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A Review—Attitudes and Aspects

Often in the practice of medicine the internist or cardiologist may be called upon to support or share with the surgeon the evaluation of the preoperative cardiac fitness of the patient undergoing an indicated surgical procedure.

No doubt, following such medical clearance, the internist has at times indulged in self-interrogation concerning the patient's chances of survival. Does the internist's responsibility hold for the period of the actual surgery, or 4, 12, or 24 hours, or a week, or a month after operation? Were the conclusions for clearance based on clinical experience inexpressible by words or on criteria of a standard text, or were they based on what may be designated as applied science of medicine, using tools—blood pressure apparatus, electrocardiograph, ballistocardiograph, etc.?

Frequently, in the course of history taking to evaluate the functional capacity of the heart, the patient would be asked how far he could walk. He might reply: "I can walk a half-mile to one mile without physical discomfort." This functional history may be the basis for the patient to be cleared for the performance of a major surgical procedure, and rightly so. Yet what would happen to this same patient should he attempt the same walk on a freezing day or a blustery, windy day? Would the weather combination represent the equivalent of a major surgical procedure?

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This variant seemed obvious to Marvin [1] in 1952, when he stated: "For every person incapacitated by heart failure, there are dozens with heart disease who are leading normal lives and many are unconscious of a cardiac lesion." We may expand his statement: The patient is unconscious of his cardiac lesion until we apply the inatrogenic elements of an electrocardiogram or the pathological findings in an overzealous consultation.

Suppose we find our patient in failure. What part does the extracardiac clinical condition, which may be a surgical disease, play in the production of the cardiac decompensation? On the other hand, in this patient in whom we have discovered electrocardiographic or physical cardiac abnormalities, will surgery trigger decompensation or a coronary occlusion; or will surgery alleviate heart failure?

The present paper was stimulated by a history related to me by a practical nurse, M., aged 54, who was, at the time contacted, doing a full eight hours' duty, performing what might be considered moderately arduous labor. She had in a previous year been a cardiac invalid, orthopneic and edematous. She was on a low-sodium diet, mercurials, and digitalis. In addition to the cardiac condition, she was suffering with recurrent attacks of gallbladder colic resulting from chronic cholecystitis and cholelithiasis. The pains were so numerous and constant that she required frequent injections of narcotics. Because of her cardiac status, operation had been denied her. There is no doubt that I and other internists would have been of the same mind and have refused her cardiac

clearance on the basis that she represented a poor surgical risk. She argued with the surgeon that a postmortem examination would be permitted after her death—but would do her no good—why not give her a chance while alive. The surgeon, against his better judgment, did a cholecystectomy. The result was the rehabilitated patient noted above. *Without the surgical disease,* she might have belonged to the category of Marvin's "people with heart disease leading normal lives unconscious of the presence of a cardiac lesion." To the internist this case would represent a medical failure in that without surgery she would have continued on under medical regimen to an early cardiac death.

Fitz-Hugh and Wolferth[2] reported a case very similar to the one described, in which the cardiac status improved after cholecystectomy. This will be further discussed below.

Let us review some of the changing trends that are related to modern medical practice.

Our population more than 65 years of age has quadrupled since 1900.[3]

From the Robert Packer Hospital, Cady[4] noted that in 1910 the average age of those undergoing operation was 28 years. Of these patients, 3% were over 70; 0.4% were more than 80 years of age. In 1951 the average age of those undergoing surgery was 40.3; 23% were above 70 and 5% were above 80. The type of surgery was not noted.

In the present paper, 204 consecutive cases having major surgery were reviewed. These cases are taken from the surgical service in a Veterans Administration Hospital, where the patient load differs markedly from that of the general population. The veteran population is predominantly male. All are above 20 years of age. Other factors are that the veteran patient is drawn from representative groups, the Spanish-American War, World War I, World War II, the Korean conflict, each group almost representing a dominant age, leaving a hiatus of age groups not serving in the armed forces because they were either too young or too old. Table 1 notes the age grouping of those receiving major surgery.

TABLE 1.—*Age Grouping of 204 Patients Undergoing Major Surgery*

Age Group, Yr.	No.	Per Cent
20-29	16	7.8
30-39	31	15.2
40-49	20	9.8
50-59	60	29.4
60-69	40	19.6
70-79	31	15.2
80-89	6	2.9
	204	

Of these 204 patients, 157, or 76.9%, were above the age of 40; 77, or 37.7%, were above the age of 60; 37, or 18.1%, were above the age of 70; 6, or 2.9%, were above the age of 80.

A total of 245 major surgical procedures were performed on the 204 patients reviewed. The procedures and their distribution were as follows:

1. Genitourinary procedures, such as partial resection of the bladder, ureterolithotomy, cystolithotomy, ureterostomy, nephrostomy, plastic repair of the kidney, and bilateral uterosigmoidostomy, nephrectomy, and cystectomy, 20 cases.

2. Gastrointestinal procedures on the upper gastrointestinal tract, including the small intestine, such as duodenostomy, jejunostomy, gastrostomy, subtotal gastric resection, total gastrectomy, resection of the jejunum, cholecystotomy, cholecystectomy, cholecystoenterostomy, gastrojejunostomy and celiotomy, 113 cases.

3. Large-bowel procedures, including colostomy, colon resection, hemicolectomy, protosigmoidectomy, resection of the sigmoid, and appendectomy, 28 cases.

4. Body-wall procedures, such as herniorrhaphy, 33 cases.

5. Orthopedic procedures, consisting of amputations and open reduction of fractures, 16 cases.

6. Miscellaneous procedures, including portacaval shunt, lumbar sympathectomy, vagotomy, splenectomy, mammaplasty, mastectomy, subtotal thyroidectomy, hysterectomy, and uterine suspension, 35 cases.

Following the completion of a surgical procedure, the responsibility borne at least consciously varies with the passing of time. The anesthetist assumes a total to partial

responsibility for the patient while on the table and from 12 to 24 hours after. The surgeon assumes responsibility of an administrative surgical death for 24 to 48 hours. Beyond that, it is difficult to assess whether the surgical procedure actually influenced the death of the patient, for there are so many factors other than the surgery itself—electrolytic imbalance, organ depression or dysfunction, toxicity of a peritonitis, the progress of malignant metastasis, senescence, and stresses—still unknown and unmeasured. The estimate of time in survival or postoperative death as related to a surgical procedure is flexible and variable. Sadove[5] found that most of his postoperative deaths related to surgery occurred within 14 days. Carp[6] enumerated his postoperative deaths related to surgery as occurring within one month after operation. We agree that one month would seem to be an adequate period in which to cancel out surgical effects. Most of the deaths noted in the present paper occurred within 10 days.

Butler, Feeney, and Levine[7] reviewed 414 cardiac patients undergoing 494 operations and divided their deaths between the inevitable and the unexpected. The inevitable deaths are those which, following surgery, occurred no sooner than if there had been no operation, as well as those which would have occurred in a matter of hours without surgery. The unexpected deaths are those which occurred from any accident of cardiac disease, such as cerebral embolism, cerebral hemorrhage, coronary thrombosis, postoperative pneumonia, and those for which there may have been an underlying circulatory disease, but, because they took place directly after surgery, were regarded as unexpected. By this differentiation, the authors were able to correct a total mortality rate of 12.1% to an unexpected mortality rate of 6.3%. Sprague,[8] conducting a similar study earlier, by not separating his cases of death into unexpected and inevitable, reported a gross mortality of 24.7%. Of 170 patients, 5 died suddenly on the table.

Carp[6] reviewed 450 bad-risk patients past the age of 60 who underwent major surgery and reported an operative mortality of 22.6%, including those deaths which occurred within one month.

Among our 204 patients undergoing 245 major surgical procedures, there occurred 25 postoperative deaths. Of these 25 deaths, 9 occurred in patients who were classified as noncardiac patients and who died bearing the diagnoses of peritonitis (2), irreversible shock (3), pulmonary thrombosis (2), aspiration pneumonia (1), and metastasis (1).

These 25 deaths represent a postoperative mortality of 12.3%. A review of the deaths revealed that 11 could have been classified as inevitable. These patients would have died without surgery, a fact which brought the postoperative surgical mortality based on unexpected deaths in the 204 cases down to 6.9%. Despite intellectual honesty, a personal factor is involved even in discriminating between unexpected and inevitable deaths. Of the 204 patients, 68, or 33.3%, bore diagnoses representing cardiac pathology and accounted for 16 deaths, or 7.8%, uncorrected for inevitable and unexpected deaths. When corrected, there were 11 unexpected deaths, representing a mortality of 5.3%.

The deaths occurring according to age groups are shown in Table 2.

Senescence

The age of 60 seems to be the universally adopted age at which a person is classified as "aged," or senescent. With our improved longevity, we may witness its arbitrary extension upward. Seventy-seven, or 37.7%,

TABLE 2.—*Distribution of Deaths by Age Groups*

Age Group	No. of Patients	Deaths	Inevitable Deaths	Unexpected Deaths
20-29	16	0	0	0
30-39	31	0	0	0
40-49	20	3	1	2
50-59	60	7	3	4
60-69	40	8	5	3
70-79	31	7	2	5
80-89	6	0	0	0
	204	25	11	14

of our patients taking major surgery would be in this senescent, or aged, group.

The postoperative deaths number 15, or 19.4% of *the aged;* when this figure is corrected by dropping the inevitable deaths, the rate is 10.4%. When dealing with the aged, we must consider some of the pathological aspects of senescence.

Senescence[9] pathologically expresses itself in the heart by an increase in subepicardial fat, thickening of the endocardium and valves, changes in size and pigmentation of the nuclei, and atrophy of the myocardial fibers, with an increase in the amount of cytoplasmic pigment. Clinically, there may be an increased vagal sensitivity, expressing itself in bradycardia. Functionally, the senile heart has diminished reserve, which may express itself in coronary insufficiency, circulatory embarrassment, or heart failure. Murmurs may be present on the basis of senescent thickening of the endocardium and valves, as related to the tortuosity and the lengthening of the aorta. An apical systolic murmur may be present on the basis of sclerotic mitral valves or left ventricular dilatation. The underlying heart disease in most instances of heart failure in the aged is arteriosclerosis. The commonest lesion is sclerosis of the coronary vessels, with narrowing and myocardial ischemia. However, heart disease of any or all causes may be present in the aged, such as pulmonary hypertension or syphilitic or rheumatic valvular lesions.

Table 3 includes all cardiac cases according to their age group and mortality within one month of operation, regardless of whether death was inevitable or unexpected, or of cardiac or noncardiac origin.

TABLE 3.—*Cardiac Patients Classified According to Age Group and Mortality*

	Age Group	No. Patients	No. Cardiac Patients	Age Group % Cardiac Patients	Mortality
Below age 60	20-29	16	0	0	0
	30-39	31	1	3.2	0
	40-49	20	2	10	1
	50-59	60	17	28.3	5
Senescence: Above age 60	60-69	40	21	52.5	5
	70-79	31	21	67.7	5
	80-89	6	6	100	0

The cases noted in Table 3 in senescence are few in number. It is obvious that the percentage of cardiac patients increases with age. The Grim Reaper, however, seems to be just as active among those at the age of 50-59 as at the age of 60-69. There is a tendency of some physicians, tempered by their own proximity to or distance from senescence, to practice a sort of mental euthanasia: "Oh, well, he has lived a full life"; and they may even truthfully add: "I would be lucky to reach his age."

Eversole,[3] writing on life expectancy in persons reaching 80-95 years of age, notes the following:

Age	Additional Life Expectancy, Yr.
80	+5.7
90	+3.3
95	+2.6

Assuming the truth of such figure, we have far more to offer the senescent patient than we may possibly have considered.

Dublin[6-10] presents statistics with reference to progressive invalidism in advancing age, published in 1941.

Ages	Invalid per 1,000
All ages	11
65-74	53.5
75-84	72.7
Above	106.2

Though these figures may not be representative today, should a revised statistic of today equal or better those figures of Dublin, then we do owe the senescent the right to add years to his life and life to his years. Should we do otherwise, we would then be practicing a form of euthanasia, which cannot be a part of the creed of medicine. Thumbnail sketches of the six patients above the age of 80 are presented.

CASE 1.—Age 82. Cardiac status: arteriosclerotic heart disease; electrocardiographic evidence of a healed posterior-wall infarct. The patient came in for treatment of arteriosclerosis obliterans bilaterally with ulceration of the lower right leg. Surgery consisted of a right lumbar sympathectomy under spinal anesthesia. This patient returned two years later for recurrence of pains in the lower extremities.

CASE 2.—Age 88. Cardiac status: coronary arteriosclerotic heart disease, compensated. There was electrocardiographic evidence of first-degree AV block with occasional premature ventricular systoles (this would suggest possible second-degree block). Diagnosis: Empyema of the gallbladder. White blood cell count was 24,200 per cubic millimeter, with a shift to the left. Cholecystectomy was abandoned for a cholecystostomy, which was performed under spinal anesthesia. He was discharged improved.

CASE 3.—Age 82. Cardiac status: arteriosclerotic heart disease; sinus tachycardia. The electrocardiogram was definitely abnormal, with displacement of the S-T segment. The patient was admitted for acute small-bowel obstruction. Surgery revealed cholecystitis, cholelithiasis with formation of a cholecystoduodenal fistula, and deliverance of gallstones into the lumen of the intestinal tract, causing obstruction. Surgery consisted of a cholecystectomy and repair of the cholecystoduodenal fistula. On the table, the patient developed auricular fibrillation and was digitalized. He was discharged improved. Had the attitude been maintained that the case was one of an inoperable malignancy (this was a preoperative clinical impression) occurring in an 82-year-old white man who was a cardiac case, and therefore a poor surgical risk, the patient would have been refused surgical intervention and gone on to an inevitable death.

CASE 4.—Age 80. Cardiac status: arteriosclerotic heart disease; multiple premature ventricular systoles; markedly thickened peripheral vessels. The electrocardiogram revealed nonspecific, flattened T-waves. There was x-ray evidence of gastric ulcer and multiple duodenal ulcers. His red blood cell count was 2,700,000; the hemoglobin 8.5 gm. %; hematocrit 25%. Surgery consisted of vagotomy, and anterior-type gastroenterostomy under gas-oxygen-ether anesthesia. He was discharged as improved.

CASE 5.—Age 83. Cardiac status: arteriosclerotic heart disease with coronary insufficiency. His electrocardiogram revealed a P-R interval of 0.23 second, first-degree AV block, and electrocardiographic evidence of ventricular enlargement. Herniorrhaphy for left indirect inguinal hernia was accomplished, with no postoperative complications.

CASE 6.—Age 82. Cardiac status: arteriosclerotic heart disease with mitral insufficiency. There was electrocardiographic evidence of right bundle-branch block. He came in with severe gastrointestinal hemorrhage. There was x-ray evidence of diverticulosis. The hematocrit was below 24%. Surgery was accomplished under spinal anesthesia, lasting 2 hours and 13 minutes, in the form of exploratory celiotomy with colostomy and endoscopy. The site of the bleeding was never found. He returned two years later with a repetition of his hemorrhage, at the age of 84. He returned two months later with severe serum homologous jaundice. Recently, at 85, he drove 100 miles for a visit to the hospital.

Agreed that this case does not represent one saved by surgery, yet major surgery was accomplished on a poor-risk patient. He belongs to Dublin's noninvalid 80-year-olds.

Conclusions based on the above-described successful cases should be tempered by the knowledge that the aged do have a decreased cardiac reserve and may have subclinical cardiac failure. They may subtly slip into shock and come out very slowly.

Digitalis should not be prescribed for the aged in tonic doses, for it may be harmful; they will require full digitalization in cardiac decompensation, though the maintenance dose may have to be reduced to avoid toxicity. Correction of anemia, malnutrition, avitaminosis, and an obstructed urinary flow may make the difference between a poor and a good surgical risk.

Hypertension

Hypertension in itself can almost be dismissed as a hazard in surgery. The surgical risk for patients with hypertension lies in the possibility that the operation itself may precipitate a breakdown in the vascular machine at one of its vulnerable spots—brain, heart, or kidney.[7,11,12] The patients usually do well.

Clinical experience[12] has shown that patients with hypertension do not bleed excessively, since most surgical bleeding is venous or capillary and vascular hypertension does not appear in the capillaries or veins. We are not discussing entities such as portal hypertension.

Hypertension has little influence upon unexpected mortality in surgery.[7,14] Butler, Feeney, and Levine, reported in 491 cases with level of hypertension above 160 systolic, a mortality of 5%, whether the systolic tension was above or below 160; however, should the hypertension be complicated by nephritis, the mortality, noted as 4.5% for the non-nephritic patients, rose to 15% for the nephritic. Their unexpected mortality varied by 1.4% between the hyper-

tensive and the normotensive, a value which was too small to assign to blood pressure.

In our group reviewed, all hypertension was associated with myocardial changes; there is, therefore, no further comment.

Arrhythmias

The problem of arrhythmias presents a hazard only in relation to the underlying disease. Premature auricular, nodal, or ventricular systoles in the normal would be unimportant. However, where there is extensive or moderate myocardial damage, fibrillation might be imminent or be precipitated. Usually a supraventricular tachycardia is regarded by the internist as being transitory. Should the rate be 120-130, then the product of the heart rate by the volume gives an increased output. However, should the ventricular rate rise to between 130 and 180, the product of the rate and volume results in a decreased output. In general, the internist does not regard supraventricular tachycardia as increasing the surgical hazard, since it is felt that it can usually be controlled or prevented by quinidine.

Sprague[8] warns against the sanguine prognosis in postoperative paroxysmal tachycardia in cases where cardiac pathology may have escaped our clinical diagnosis. Lyons[15] makes a statement that the prophylactic administration of quinidine has fallen from favor, because of undesirable side-effects and because of the growing conviction that cardiac arrest in the presence of quinidine therapy is especially refractory to restoration of cardiac rhythm by massage. Regardless of this attitude, it is still comforting to know that we have the therapeutic measures to control supraventricular tachycardia. There is the reflex vagal control by stimulation in which the carotid sinus pressure is increased physiologically by massage in that area. The enthusiasm for pressure on the eyeballs has been dampened by the report of retinal separation[16] caused by this barbaric maneuver. Other worthy measures are the Valsalva maneuver, carried out by maintaining a forced expiration with a closed glottis for 15 to 20 seconds; induction of vomiting either by mechanical stimulation of the pharynx or by the use of ipecac in the form of ipecac syrup U. S. P., 4 to 8 ml. Should this last measure be ineffective, it may be repeated in 45 minutes.

Parasympathomimetic drugs are used for a therapeutic response: acetylcholine, 20 mg. intravenously. If there is no reversion in three minutes, it may be repeated at three- to four-minute intervals in successively increasing doses—40, 60, 80, 100 mg. Methacholine (Mecholyl)[17,18] is also used, but, because death has been attributed to its use, my experience here remains limited. Atropine is its antidote. Phenylephrine (Neo-Synephrine) hydrochloride, 0.5 mg. intravenously, may be effective through its pressor effect increasing the blood pressure in the region of the sinus and aortic arch, with reflex slowing of the heart. Should there be no significant rise in blood pressure, then 20 minutes later, 1 mg. may be given[18,19] intravenously. Hypertension and coronary artery disease are the contraindications to the use of phenylephrine. Cedilanid (lanatoside C, N. F.) is increasing in popularity as the drug of choice in the treatment of supraventricular tachycardia. It is given in the dose of 0.8 mg. intravenously. This may be repeated in one hour, with a total dose of up to 1.2 to 1.6 mg.

Carotid sinus pressure may be reapplied concurrently with any of the therapeutic measures.

Ventricular Tachycardia

Ventricular tachycardia presents increased surgical hazard, since it is usually evidence of structural heart disease, particularly coronary artery disease. Quinidine has been the standby not only in auricular tachycardia but also in ventricular tachycardia. Since 1951 the antiarrhythmic qualities of procainamide hydrochloride (Pronestyl) has been added clinically to our armamentarium.

Quinidine sulfate may be prescribed as follows[19]: give 0.2 to 0.4 gm. every two hours for five doses on the first day, and, if indicated, increase the unit dose by 0.2 gm. every two hours for the second day for five doses, and again increase the unit dose by 0.2 gm. every two hours, for a maximum five doses on the third day. Another therapeutic method of using quinidine is the method of Levine, giving 0.2 gm. for the first dose and increasing each successive dose by 0.2 gm. every four hours, until the desired effect is achieved.

The combination of morphine and quinidine has been found effective.

Procainamide may be prescribed by mouth: 0.25 to 0.5 gm. repeated in two hours. This dose would be effective for cardiac irritability. There is no specific dose for ventricular tachycardia. Orally, 1.25 gm. is prescribed initially, followed in one hour by 0.75 gm. and then by 0.5 to 1.0 gm. every hour. Intramuscularly, one gives 1.2 gm. initially, followed by 1 gm. every one to three hours.

The intravenous method is used only where severe hypotension exists, then in a dose of 0.25 to 1 gm. at a rate of 100 mg. per minute every 30 to 60 minutes, until an effect is obtained.

Whether we use quinidine or procainamide, an electrocardiogram is a necessary adjunct to differentiate correction, persistent tachycardia unrelated to drug, or a toxic result. As to which to use, one may say that there is not yet enough experience to judge between procainamide and quinidine as the better drug. The drug of one's experience should be the drug of choice.

Fibrillation

Atrial fibrillation is most frequently seen in rheumatic heart disease, arteriosclerotic heart disease, and hyperthyroidism. Both the paroxysmal and the chronic types, however, may be seen in the absence of organic heart disease. Atrial fibrillation in itself does not increase the surgical risk, providing the ventricular rate remains below 100. The increased surgical hazard[12] is that of the underlying heart condition. If it is paroxysmal[20] and of short duration, its reversion by quinidine may be considered. If of more than three months' duration, its reversion may be temporarily successful. Our interest here lies in maintaining a ventricular rate of 60 to 70 per minute. The same system of quinidinization[19] may be used, as noted earlier. For the patient with chronic fibrillation with rapid ventricular rate, digitalization is indicated. The surgeon does not prefer the quinidinization or digitalization of the patient as a routine.

Conduction Defects

AV block[1,21] not associated with the Adams-Stokes syndrome does not increase the surgical hazard; AV block accompanied by Adams-Stokes syndrome greatly increases the surgical hazard.

Delayed conduction[22] itself may be precipitated by anoxemia or drugs, such as ether. Delays in AV conduction will occur in 50% of the patients under ether anesthesia, whereas ventricular rhythms (tachycardia or fibrillation) are rare under ether.

Bundle-branch block[23] in itself has been given a poor prognosis. The prognosis for bundle-branch block has been cited as three to five years from the date of diagnosis. However, the initial studies were on people with known cardiac disease. The commonest cause of bundle-branch block is coronary artery sclerosis, although there are less frequent causes, such as rheumatic myocarditis or myocarditis associated with systemic disease or congenital heart disease with interventricular septal defect. Routine electrocardiographic studies of normal subjects, particularly in the field of aviation, revealed increasing numbers of patients with electrocardiographic evidence of bundle-branch block without other evidence of cardiac abnormality.

The finding of a bundle-branch block would indicate widespread changes in the myocardium, or it may be the result of a myocarditis *long since past and completely*

healed. The prognosis of bundle-branch block is therefore based on the etiology and severity of the underlying condition, and not on the electrocardiogram.

Barker [23] does not believe that the cardiac reserve in bundle-branch block is decreased, since the timing of systole and diastole of either ventricle remains individually unchanged. Again, the electrocardiogram by itself has no prognostic value.

As for the relationship of bundle-branch block to surgery, this abnormality has been considered an increased surgical hazard. However, the trend now is to consider it as a hazard only on the basis of the underlying cardiac condition.

At Memorial Hospital,[24] 59 patients, between the ages of 66 and 71, having bundle-branch block about equally divided between the right and the left side (the usual statistical relationship) received major surgery. They had an immediate mortality of 10% in 19 days—half of this 10% were medical deaths, and three were unrelated to the heart. In five cases there was evidence of progression of heart disease. The underlying condition of the senescent patient with bundle-branch block is arteriosclerotic heart disease.

Our series consisted of 15 patients with bundle-branch block among 68 cardiac cases. Of these, two died within 2 days, and one died by the 20th day, representing a mortality of 20%. Yet if one should investigate further, one would find factors which would in themselves be the reason for considering the patients as poor surgical risks, other than the presence of bundle-branch block.

Case 7.—Age 43. History of coronary occlusion with residual infarction, bundle-branch block, and chronic coronary insufficiency. Surgery consisted of a cholecystectomy, followed by an unexpected death in five days—a cardiac death.

Case 8.—Age 65. Arteriosclerotic heart disease with electrocardiographic evidence of left bundle-branch block. This patient had an adenocarcinoma of the cardiac end of the stomach, with metastasis to the esophagus, lymph nodes, and peritoneum. Surgery consisted of transthoracic total gastrectomy, splenectomy, resection of the tail of the pancreas, and esophagojejunostomy. He died six days after operation with pneumonia, right lower and middle lobes. His case represents an inevitable death.

Case 9.—Age 64. History of four episodes of acute myocardial occlusion in the past. When seen, he had evidence of decompensation, crepitant rales in both bases, and electrocardiographic evidence of left bundle-branch block. He was on digoxin. Although he was considered a poor surgical risk on the basis of decompensation, surgery was done for acute appendicitis. He died on the second postoperative day: a cardiac death.

The attitude toward bundle-branch block as a surgical hazard should be that of the underlying myocardial disease, if it is present.

Coronary Disease

The problem of major surgery in patients with coronary disease resolves itself with logic. Patients with acute coronary occlusion are poor operative risks and should not be operated upon except in absolute emergency. This type of lesion produces the highest mortality,[7] mentioned as high as 80%. Butler, Feeney, and Levine,[7] in their series, had 41 operations on 35 patients having angina pectoris, with 3 unexpected deaths, or a mortality of 7.7%. In 20 operations performed on as many patients with coronary thrombosis, there were 8 unexpected deaths, or a mortality of 40%. In a report from the Mayo Clinic,[26] Brumm and Willius state that only 11, or 4.3%, of a series of 257 surgical patients with severe coronary disease died of purely cardiac causes after operation: average age 60. Thirty-two gave a history of previous coronary thrombosis.

In a report from Robert Packer Hospital, Cady [4] reports 58 cases of healed myocardial infarctions with an operative mortality of 5.2%, as compared with a mortality rate of 3.4% among 260 noncardiac patients between the ages of 60 and 70 years.

Ilgenfritz [25] reports the operative risks in patients healed, with fibrosis, over a period of months have a reported mortality of 15%. Authors vary in their recommendations for the period of waiting for surgery, from 90 days to 4 or 8 months following the acute occlusion. Individual clinical judgment should decide here.

Coronary occlusion [12] is one of the postoperative complications to which cardiac patients, especially those in the older group, are subject. Peripheral vascular collapse, such as occurs frequently following surgery, may precipitate a coronary occlusion.

Hannigan [27] et al. made an analysis of the cardiorespiratory complications, which would include coronary occlusion. Among their patients they noted occurrence of such complications in 43% of the patients who were given thiopental (Pentothal) sodium, 27% in those receiving ether, 8.3% in those receiving spinal anesthesia and zero in those receiving local anesthesia.

The length of time of the performed surgery was of interest. When the surgery lasted less than one hour, there were no cardiorespiratory complications; if the surgery lasted less than two hours, there were complications in 13%; if between two and three hours, there was an incidence of 31.6%; if longer than three hours, there were complications in 37%. Those receiving 1,000 cc. of blood or 3,000 cc. of fluid would have the same rate of cardiorespiratory complications as surgery lasting up to two hours.

In reviewing our own figures for operative time we found 25 deaths among the cardiac and noncardiac patients. Only 6 had operative times up to two hours; the remaining 19 had surgery lasting beyond two hours, up to eight hours. Among the 52 surviving cardiac patients, only 12 had surgery lasting beyond three hours; 11 had surgery lasting two to three hours. The remaining 29 had surgery lasting between one and two hours. Among those six patients over the age of 80, only one had surgery lasting more than two hours. There were no deaths. It would appear that length of time is a factor in survival.

There are simple principles in dealing with a patient with a past history of myocardial infarction. They are (1) adequate preoperative rest; (2) sedation; (3) reassurance; (4) attention to anemia, avitaminoses, hypertension, and diabetes; (5) (important) avoidance of pre- and postoperative anoxia; (6) (very important) maintenance of adequate blood pressure during and after surgery.

The duration of the surgical procedure directly affects the occurrence of cardiorespiratory complications and survival.

Cardiac Decompensation

There is no doubt that cardiac decompensation is a hazard, and there is general agreement that if it is possible, steps should be taken to have the patient compensated at least three weeks prior to the contemplated surgery. However, despite the presence of congestive failure, one may be called upon to accomplish major emergency surgery. All the internist can offer at that time is an opinion that the patient is a poor surgical risk and recommend the following regimen.

If the patient has not been taking digitalis, rapid digitalization is indicated. Ouabain (crystalline strophanthin from Strophanthus gratus), 0.3 mg. intravenously, followed by 0.1 mg. every half-hour, not to exceed 1 mg., is given until a therapeutic result is noted. This method has its adherents; however, this method belongs to the most experienced. A safer method is lanatoside C, N. F. (cedilinid), 0.8 to 1.2 mg. intravenously, followed, if necessary, by a dose of 0.4 mg. every four to eight hours until a therapeutic result is attained. Another method is the intravenous use of digoxin, 0.7 to 1 mg. If therapeutic result is not obtained in six hours, then 0.25 to 0.5 mg. is given every six hours. The daily maintenance dose may be started on the day following. Every effort should be made to postpone surgery one, two, or three hours during the digitalizing phase. Should the patient present himself in congestive failure, despite having been on digitalis and other decongestive measures, and surgery will be done despite cardiac status, then the recommendations are for good oxygenation (100% oxygen given at the rate of 8 liters per minute), strict balance between blood loss and blood

replacement, and electrolytic and fluid infusions based on basal need and replacement, although it must not be overlooked that this patient may have a hyponatremia or hypokalemia resulting from the treatment of this congestive failure. There can be no set rule, and the treatment will have to fit the case.

Despite the morbid prognosis alluded to in relation to surgery performed on patients in cardiac decompensation, there are some results borne out by clinical experience in that the removal of a source of ill health,[12,25] such as a chronically diseased gallbladder or an abdominal hernia, will not only correct the local disturbance but also bring about a marked improvement in the cardiac status. Apparently, the operation will relieve the heart sufficiently to enable it to acquire its compensation. It is as though one were to say that it might be desirable to perform an operation of election to accomplish this aim.

The results in surgery of the thyrocardiac patients—with the reversal of congestive failure following subtotal thyroidectomy—and the improvement accompanying surgery for constrictive pericarditis are already familiar to us and are not under discussion.

In the introductory phase of this paper, a case was described of a cardiac invalid who was rehabilitated after surgery of the gallbladder. The following case, though less remarkable in its rehabilitation, is also somewhat illustrative of improvement following surgery.

Age 71. The patient came into the hospital in December, 1953, with the diagnoses of arteriosclerotic heart disease, myocardial damage, decompensated Class 4 diabetes mellitus, mild, and a right inguinal hernia. He had been a patient three months earlier with the same diagnosis but returned because the family physician had been unable to control his edema. Despite the use of mercurial diuretics, he had become increasingly edematous. The edema was present in the region of the sacrum and scrotum. The chest was emphysematous; crackling rales were present at the bases; blood pressure was 108/74. His heart was slightly enlarged; sounds distant; P2 louder than A2; soft systolic murmur at the apex; frequent extrasystoles. The liver edge was 5 fingerbreadths below the right subcostal margin. There were gross anasarca of the lower extremities and 4+ pitting edema of the sacrum.

As for his course in the hospital, he was started on a dehydrating regimen without success. Ascites began to develop. Many of the features in the case suggested cirrhosis of the liver. A sulfobromophthalein Bromsulphalein) test revealed 45% retention at the end of 60 minutes, but this could have been due to dysfunction related to a congested liver. Total protein was 5.5 gm. %; albumin 3.8 gm. %, and globulin 1.65 gm. %. Throughout January, 1954, he had various modifications of dehydration, including acetazolamide (Diamox) and the carboresins. In February, 1954, the patient's condition worsened; he had a right pulmonary effusion. A thoracentesis was accomplished, and 700 cc. of straw-colored fluid was removed. The cardiac service was conscious of potential sodium or potassium deficiencies. On March 22, 1954, a left strangulating femoral hernia developed, which required emergency surgery. The patient's blood pressure was 90/50; the pulse was grossly irregular; peripheral edema was marked, and rales were present in the chest. He was given dextran and some saline. Surgery was done under local and thiopental (Pentothal) sodium anesthesia. Twelve inches of small intestine was resected.

On the second postoperative day, the patient's edema completely disappeared, and as time went on the abdomen remained flattened; the ascites had disappeared.

On April 29, 1954, the patient went into a circulatory collapse, the blood pressure dropping to 50/0. For a while he was in what seemed to be irreversible shock. Eventually, his blood pressure rose moderately, and he was able to be discharged as improved, without edema, with the diagnosis of arteriosclerotic heart disease, normal sinus rhythm, cardiac functional capacity, Class IV, improved.

This case represents a hazardous surgical risk in which congestive failure was reversed beyond expectation after removal of a source of ill health.

Fitz-Hugh and Wolferth[2] discuss the problem of cardiac improvement following gallbladder surgery. In their discussion they presented cases in which the removal of gallstones, preferably by cholecystectomy, had been followed by restoration of a cardiac compensation in a few cases of chronic congestive failure, with marked amelioration, and sometimes cure, of more or less incapacitating angina, or what appeared to be a major attack of coronary occlusion. They report six cases in which initially surgery was refused on the basis of the patient be-

ing a poor surgical risk. One woman, at the age of 64, who had been refused on the basis of severe coronary disease, had her surgery done during an attack of epigastric pain and jaundice. She survived to have her anginal attacks disappear and to have reversal of her inverted T-waves. Furthermore, she was able to lead a normal life and play golf.

The six patients they report were cardiac invalids in whom surgery of the gallbladder was done, followed by a return to practical normal health, with electrocardiographic improvement.

Beckwith et al.[28] also present a study of the relationship of gallbladder and heart disease. A review of the literature revealed that the autopsy incidence of gallbladder disease in patients with coronary artery disease varied from 17.5% to 48.8%, while the incidence in patients without coronary disease was about 11.5%. In 26,499 hospital admissions, 6.8% to 7.5% of the patients with clinical coronary sclerosis (angina or infarction) had cholecystitis, as compared with the incidence of 1.7% of cholecystitis in patients without coronary disease. Arrhythmias, including heart block, ventricular tachycardia, and cardiac standstill, have been produced by distention of the bile duct.

McLemore and Levine[29] describe six patients between the ages of 47 and 72 who had Adams-Stokes syndrome. Following cholecystectomy there was striking improvement. The follow-up period was 6 months to 12 years.

Despite the glowing reports on cholecystectomy reversing heart failure syndromes, not all patients with associated gallstone disease and heart disease are benefited by gallbladder surgery. Catastrophic coronary occlusion may occur during an attack of cholecystitis or choledochitis, and during or after surgery for relief of the gallbladder disease.

The case of D. is presented to illustrate the darker, or adverse, results of good intentions and good clinical judgment. He was 43 years old. He had his first coronary occlusion at the age of 41. Despite the healing of the infarct, he had persistent pains of coronary insufficiency. He was also found to have cholelithiasis and chronic cholecystitis. He had two types of pain—the anginal pain, relieved by glyceryl trinitrate U. S. P. (nitroglycerine), and a second pain at the lower end of the sternum, radiating to the right subcostal region, not relieved by glyceryl trinitrate. Serum cholesterol was 425 mg. %. The electrocardiogram revealed elements interpreted as being consistent with coronary insufficiency. It was felt that the gallbladder disease triggered the repeated attacks of angina, and, with that thought in mind, he was transferred to the surgical service for a cholecystectomy to eliminate the gallbladder disease and colic and, secondarily, to improve his cardiac status. A cholecystectomy was done under high-spinal anesthesia. The procedure lasted two hours. Upon his return to the ward, his blood pressure was considered adequate. Twenty-four hours later his blood pressure fell to the systolic level of 74 mm. Hg. The electrocardiogram revealed supraventricular tachycardia and evidence of a right bundle-branch block. He died on the second postoperative day, and postmortem examination revealed a massive infarct.

Morrison and Swalm[30] were conscious of the relationship of the gastrointestinal tract to the heart and include in their discussion instances in which cardiospasm would cause heart block and auricular fibrillation, as well as an instance of cardiospasm resulting in sudden death in which the autopsy revealed no cause. An instance is reported of a patient who would faint regularly from heart block caused merely by swallowing. This was controlled with atropine. Morrison and Swalm[30] noted that they had indifferent results from the usual methods of management of angina pectoris; so they resorted to intensive treatment of the gastrointestinal tract, with better clinical results.

It is beyond the scope of this paper to describe the overlapping viscerosensory pathways of the autonomic nervous system. Very briefly—aside from the stomach innervations by the right and left vagus nerves—it receives branches from the celiac plexus of the sympathetic trunk. The greater splanchnic nerve terminates in the celiac ganglion. This has branches that can be traced in the sympathetic trunk as high as the first and second thoracic sympathetic ganglion, which are among the direct trans-

mitters of sensory pathways for pain in the heart.

Clinical evidence of this overlapping is noted during surgical procedures by sudden drops in blood pressure during the handling of viscera. Smith [31] calls it the celiac-plexus reflex, which is a vagotonia that can be reversed by atropine.

Similar reflexes [32] take place in intrathoracic surgery during periosteal rib scraping, rib spreading, pleural incision, especially in the hilar region, where one may get maximum vagal stimulation, producing asystole; mechanical stimulation of the smaller bronchi produces slowing and temporary standstill of the heart.

Often the heart is held culpable for the collapse of a surgical patient when, in fact, the heart was struggling to compensate for the true cause of the calamity—a peripheral circulatory failure. The primary shock may be reversible, but the secondary shock, delayed prolonged shock or true shock, may be insidious in its outset, and be unrecognized. The pathophysiological elements entering into shock are complex, but it will manifest itself in an ineffective blood volume, hypotension, and tissue anoxia, which requires immediate and active therapy. The active therapy may be 500 cc. of plasma, repeated every half-hour up to a total of 2 liters, or whole blood if anemia or blood loss is a factor. Plasma expanders are of value for those fearing a serum homologous jaundice or considering economy. Levarterenol (Levophed) bitartrate may be used, 4-16 mg. diluted in 1 liter of 5% dextrose, flowing at a rate of 20-40 drops per minute to maintain blood pressure. It has been our unfortunate experience to witness the occurrence of gangrene and sloughing in the infusion area when levarterenol has been used to support the patient for many days. So when prolonged shock therapy is anticipated, phenylephrine hydrochloride (Neo-Synephrine) 100-150 mg. per liter of 5% dextrose, water, may be given slowly, with the rate of flow judged by the response.

We may be dealing with a patient who has already given maximum response and cannot be further stimulated. Adrenocorticosteroid therapy may be used for what it may be worth. It can be spectacular. It can be given as hydrocortisone, 100-150 mg. diluted in 1,000 cc. of 5% dextrose or saline by slow drip. Unfortunately, despite such measures, the patient may not respond, and may die in irreversible shock. Treatment of others in prolonged shock suggests that unremittent, dogged, continuous therapy may be rewarded by the patient's survival.

Continued anoxia of tissues, especially when producing a coronary insufficiency, may precipitate a coronary occlusion or infarction, which would be recognized at the autopsy table, with the blame or cause of death being put on the heart.

Conclusions

A review of 204 cases, having a total of 245 major surgical procedures, is presented.

Among the 204 cases, there was a corrected mortality of unexpected deaths amounting to 6.9%.

A greater percentage of major surgery is being done in the aged, and the mortality and prognosis are keeping in step with the factors improving longevity.

The surgical hazard of bundle-branch block is that of the underlying condition, since bundle-branch block itself may not decrease the myocardial reserve of the ventricle.

Coronary occlusive disease is still a hazard in the performance of major surgery, which decreases with the healing of time.

An extracardiac diseased organ may be the stress causing myocardial or coronary failure. Unusual clinical judgment or luck is needed to solve this problem.

Postoperative shock or death does not indicate that the internist or practitioner has misjudged the heart as a major surgical risk, for there are still physiological extracardiac components beyond present knowledge and understanding, causing peripheral collapse.

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Simplified Technique for Correcting Umbilical Hernias in Infants and Children*

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The umbilical hernias which persist despite faithful and persistent strapping with adhesive tape during the first year of life usually require surgical correction. Troublesome umbilical hernias and those in patients who cannot be treated by adhesive strapping, either because their skin will not tolerate it or because their parents fail to cooperate, may require correction before reaching the age of one year.

The simplified technique illustrated here is entirely adequate. It has been amply tested over the past 10 years, and there have been no significant complications. No hernias have recurred in private patients. In service patients complete follow-up has not been possible, but as yet there are no known recurrences.

Most defects in umbilical hernias are either round or oval, with the longer dimension transverse. Extensive dissection to permit separate closure of peritoneum and hernial sac is unnecessary. The two layers can be used as one to close the defect without tension. To excise and discard the fibrous layer of the hernial sac and approximate the edges of the rectus sheaths under tension likewise seems unwarranted, since nonoperative closure of the umbilical defect is due to the contraction of this tissue as a part of the ultimate umbilical scar.

The illustrations show the technique in detail.

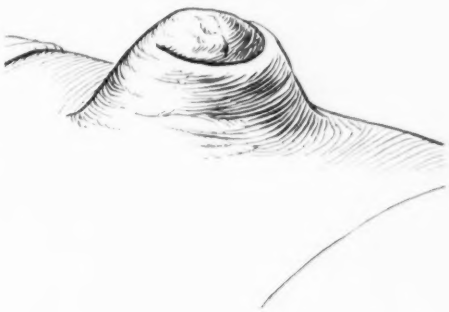

Fig. 1.—Protrusion of an umbilical hernia in a recumbent year old child. The incision is placed in the natural skin fold inferiorly.

* Surgery Illustrated.

From the Departments of Surgery, Stritch School of Medicine of Loyola University, Mercy Hospital, and Cook County Children's Hospital.

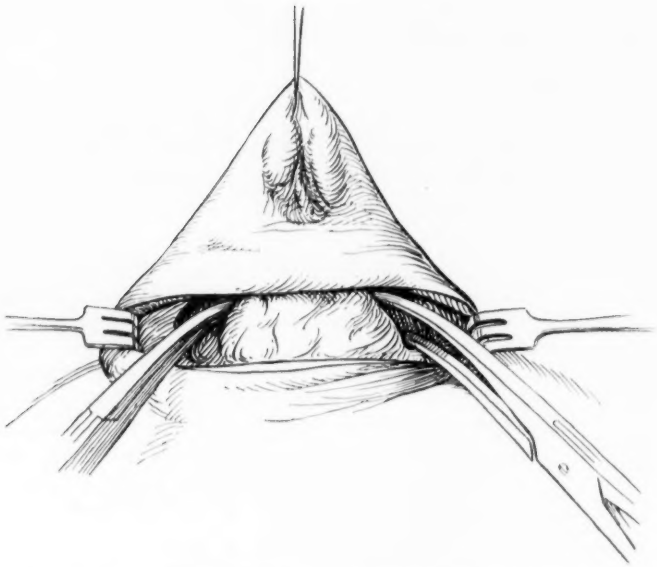

Fig. 2.—The hernia sac is partially exposed. The sac is completely freed from the surrounding tissue by blunt dissection with a curved Kelly forceps.

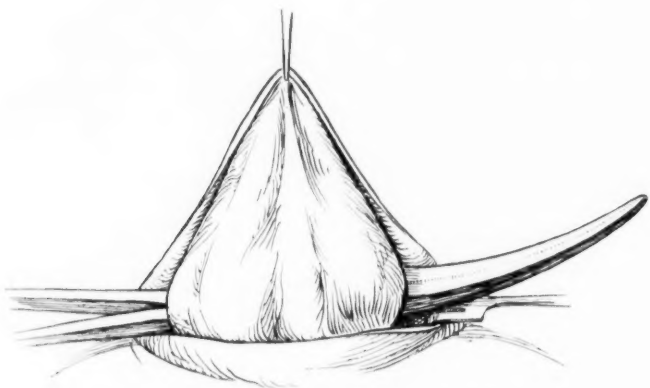

Fig. 3.—The sac is isolated by passing the forceps behind it. Palpation of the sac against the clamp aids in determining the presence of unreduced contents.

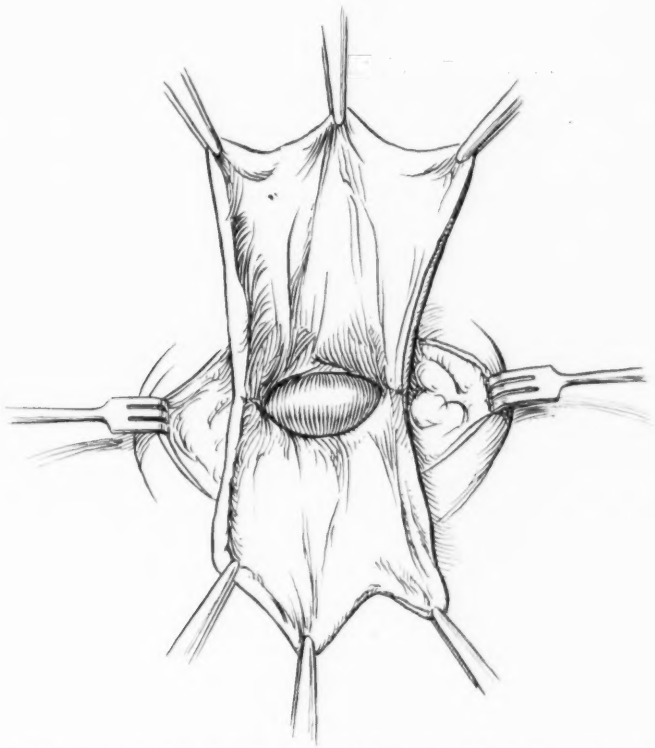

Fig. 4.—The sac has been opened and dissected free of umbilical skin with a finger in the sac as a guide. Upper and lower flaps have been made of the full thickness of the hernia sac by lateral incisions down to the level of the rectus sheaths.

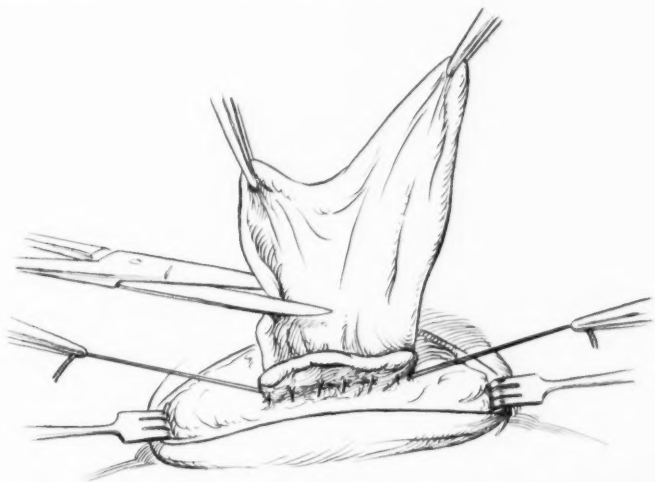

Fig. 5.—The umbilical opening is closed by a row of mattress sutures of silk approximating the upper and lower flaps of the hernial sac. The redundant portion of the inferior flap has been excised.

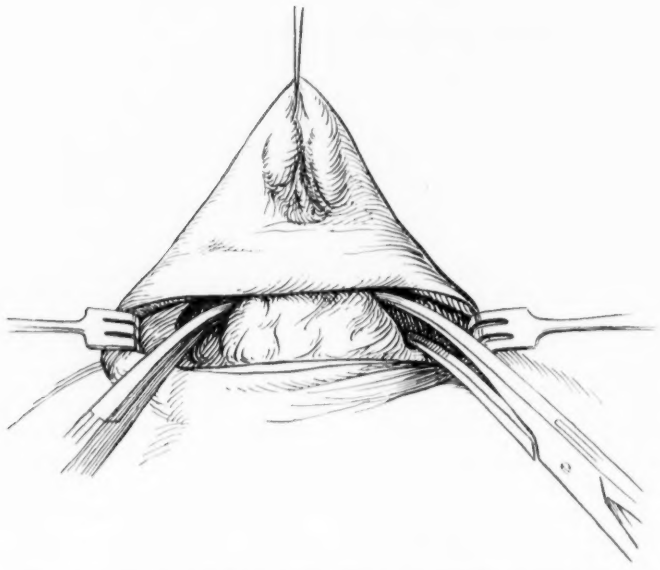

Fig. 2.—The hernia sac is partially exposed. The sac is completely freed from the surrounding tissue by blunt dissection with a curved Kelly forceps.

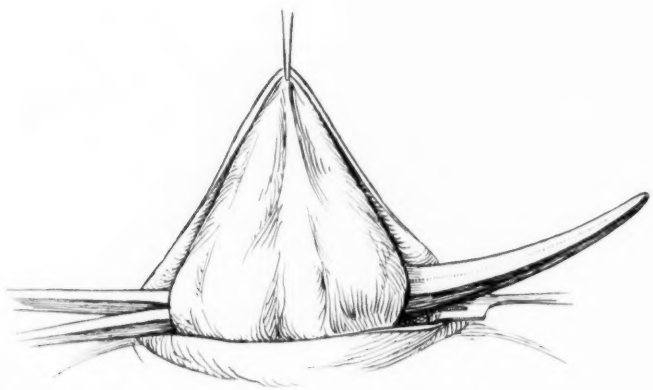

Fig. 3.—The sac is isolated by passing the forceps behind it. Palpation of the sac against the clamp aids in determining the presence of unreduced contents.

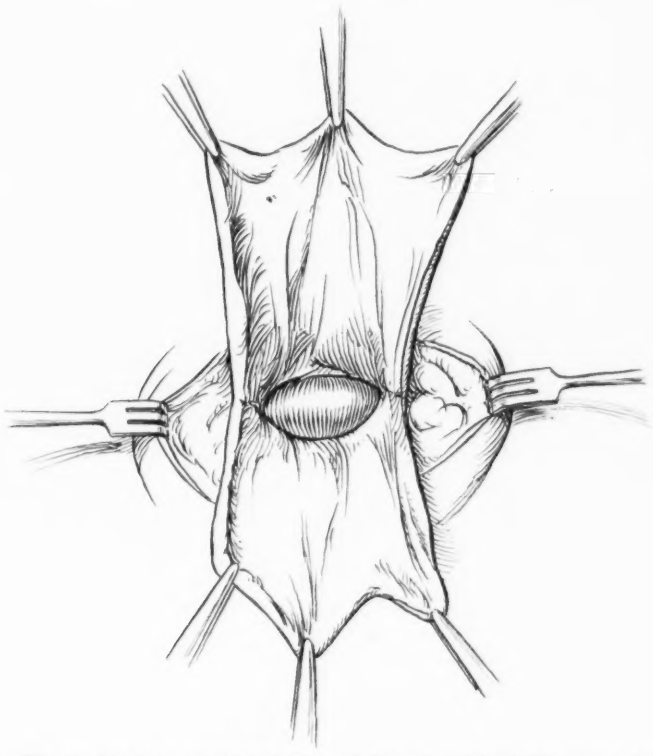

Fig. 4.—The sac has been opened and dissected free of umbilical skin with a finger in the sac as a guide. Upper and lower flaps have been made of the full thickness of the hernia sac by lateral incisions down to the level of the rectus sheaths.

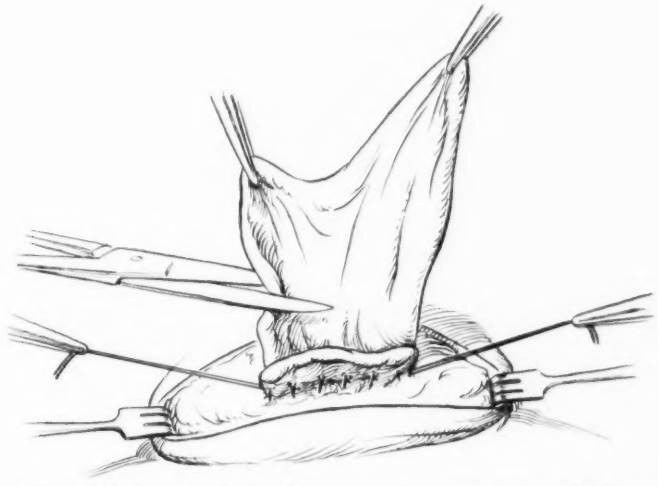

Fig. 5.—The umbilical opening is closed by a row of mattress sutures of silk approximating the upper and lower flaps of the hernial sac. The redundant portion of the inferior flap has been excised.

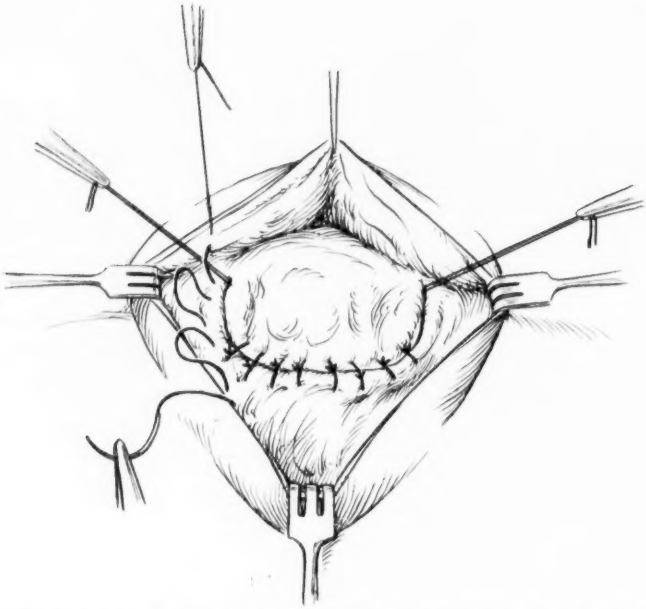

Fig. 6.—The upper flap has been brought down over the first suture line in a "vest over pants" type of repair. The edge of the overlapping upper flap is sutured to the rectus fascia by interrupted silk sutures. The wound is closed by three or four absorbable (gut) sutures which "purse string" the subcutaneous tissue in the sagittal plane and catch a bit of the rectus fascia and the layers of the hernial sac to obliterate the dead space and to fold the redundant skin.

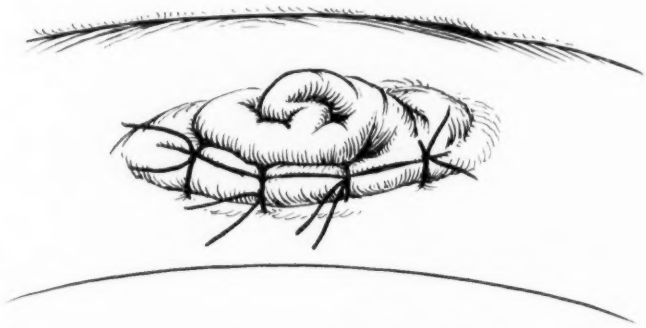

Fig. 7.—Subcuticular sutures of fine gut or interrupted silk sutures approximate the skin edges. Benzoin tincture is applied to the surrounding skin. A dry gauze dressing small enough to cover only the operative area is held in place by a patch of adhesive tape.

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Perforation of Dura by a Plastic Catheter During Continuous Caudal Anesthesia

WILLIAM HAMELBERG, M.D.; JOHN SIDDALL, M.D., and LEON CLAASSEN, M.D., Columbus, Ohio

Occasional perforation of the dura is a well-recognized possibility following the insertion of a needle into the caudal canal. Perforation of the dura by a plastic catheter passed through a needle in the caudal canal is rare. A review of the literature discloses several reports of dural perforation using malleable needles, but none following the use of a plastic catheter. The following is a case report of such an occurrence.

Report of Case

The patient, a 60-year-old man, was admitted for elective repair of bilateral inguinal hernia. The past history was relevant in that 43 years prior to admission the patient had had rheumatic fever, resulting in rheumatic heart disease. At the time of surgery, he had mitral stenosis and atrial fibrillation without evidence of cardiac failure. An electrocardiogram showed left ventricular hypertrophy, auricular fibrillation, premature ventricular extrasystoles, and an old posterior myocardial infarct. All other physical and laboratory examinations were within normal limits.

Continuous caudal anesthesia was chosen for the patient. This choice was based upon the decreased cardiac reserve of the patient and his physical build, which facilitated insertion of the caudal needle. Preoperative medication consisted of pentobarbital sodium U. S. P. (Nembutal), 100 mg., and meperidine (Demerol) hydrochloride U. S. P., 75 mg. The patient arrived in the operating room under adequate sedation, with a blood pressure of 110/80 and a pulse rate of 80 a minute.

An 18-gauge thin-walled caudal needle was inserted into the caudal canal without difficulty. After aspiration to ascertain that the point of the needle was neither in a blood vessel nor in the subarachnoid space, a test dose of 4 cc. of 1% lidocaine (Xylocaine) hydrochloride U. S. P. was injected. No evidence of spinal anesthesia resulted from the test dose, and a plastic catheter was introduced through the needle to a point 4 cm. beyond the end of the needle. The end of the catheter was blunt.

After the catheter was secured, 10 cc. of 1% lidocaine hydrochloride was injected. Profound anesthesia up to the umbilicus developed in less than one minute. Surgery was begun and proceeded uneventfully. Thirty minutes after the first dose, an additional 10 cc. of lidocaine hydrochloride was given. Immediately after the second dose, the blood pressure fell to 90/60, and the patient became cyanotic. Because of the patient's impaired cardiac status, this level of blood pressure was considered inadequate. The patient promptly responded to treatment with an infusion containing 3 mg. of phenylephrine (Neo-Synephrine) hydrochloride in 200 cc. of 5% dextrose in water. The cyanosis cleared when oxygen was administered by a mask placed on the patient's face, and his respiration was assisted by intermittent pressure on the breath-

Radiograph following injection of 1 cc. of iophendylate (Pantopaque). *A*, plastic catheter in caudal canal; *B*, iophendylate in the subarachnoid space.

Submitted for publication Aug. 15, 1958.

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Present address: Medical College of South Carolina, Charleston, S. C. (Dr. Hamelberg).

ing bag. No additional lidocaine was given, and the operation ended 90 minutes after starting. The level of anesthesia at the end of the procedure was at the xiphoid.

After operation, clear fluid was noted to be accumulating in the syringe attached to the catheter. This was believed to be spinal fluid, and the finding of 10 mg. % protein in the fluid tended to verify this belief.

To identify the location of the catheter more accurately, 1 cc. of iophendylate (Pantopaque) was injected through it under fluoroscopy. The dye was noticed to move freely in the spinal fluid. This finding confirmed the impression that the catheter was in the subarachnoid space (Figure). The patient's postoperative course was entirely uneventful.

Comment

Although a test dose of local anesthetic drug was given after introduction of the caudal needle, another test dose should have been given after the insertion of the plastic catheter. The prompt and profound anesthesia which developed after the small initial dose was unrecognized as indicating the possibility of a subarachnoid injection.

The common complications of spinal, caudal, and epidural anesthesia are respiratory depression or arrest and hypotension. These can be simply and effectively treated by artificial respiration with oxygen, and by the intravenous administration of a vasopressor drug.

Summary

After a test dose of local anesthetic drug, which indicated that the caudal needle was not in the subarachnoid space, a plastic catheter was inserted. It pierced the dura and spinal anesthesia resulted. The location of the catheter was verified by radiography. Prompt resuscitative measures resulted in a satisfactory outcome.

Medical College Hospital, Medical College of South Carolina, Charleston, S. C.

Correction

In the article, "Primary Multiple Cancers," by Dr. B. M. Fried published in the November issue of the ARCHIVES, the last paragraph should read:

It is desirable to divide primary multiple cancers into two categories: (1) those which originate in organs of the same system, and (2) those which arise in organs of different systems. The multiplicity of cancers of the first category is due in all probability to a predisposition *sui generis*, while the advent of two or more cancers in the second category is due very likely to a mere coincidence.

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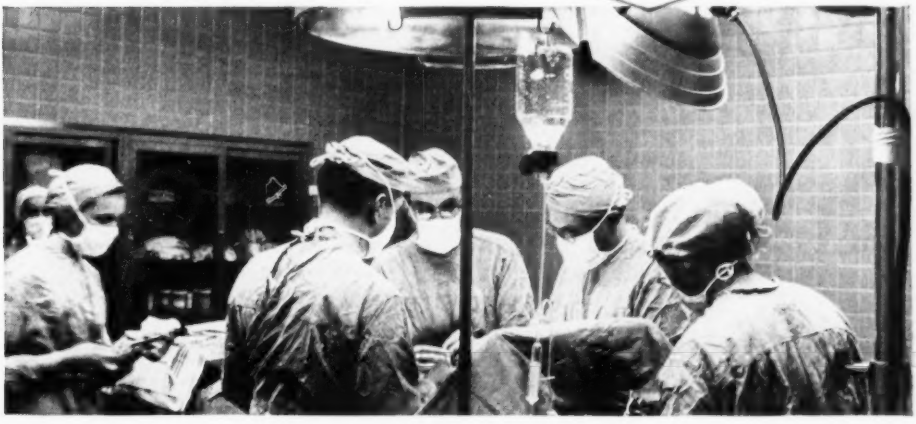

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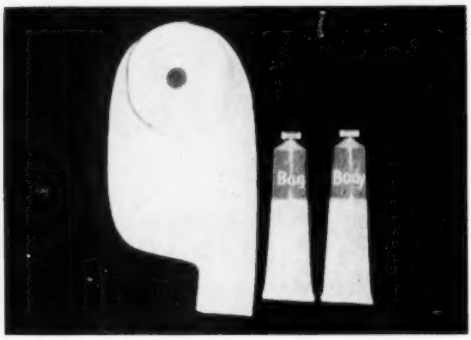

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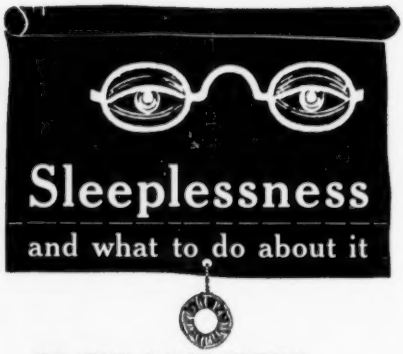

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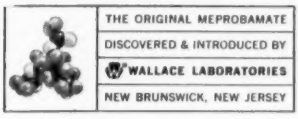

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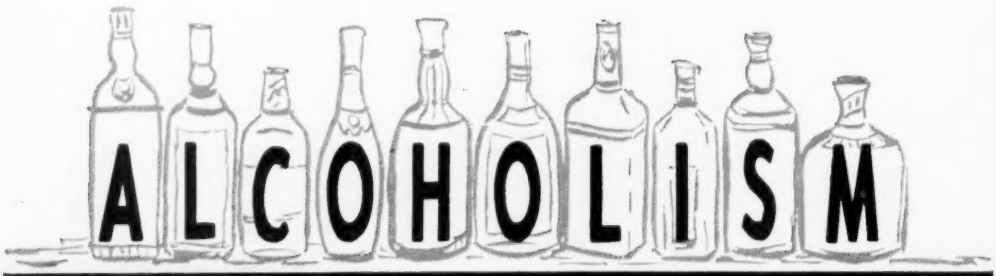

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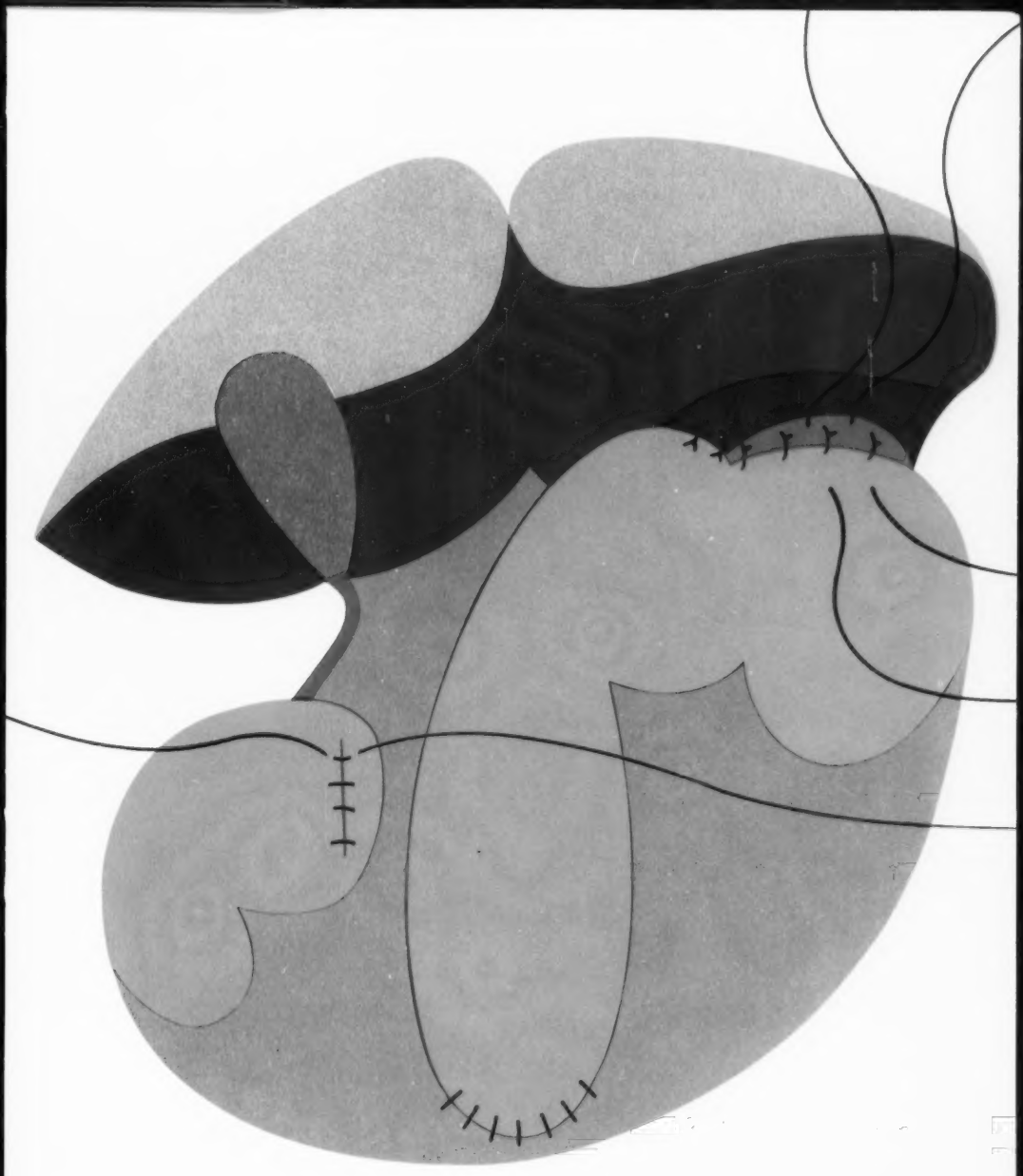

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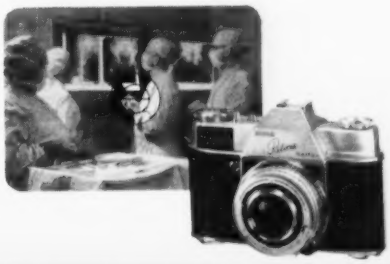

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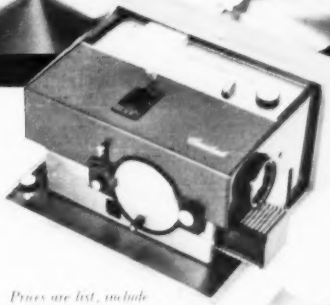

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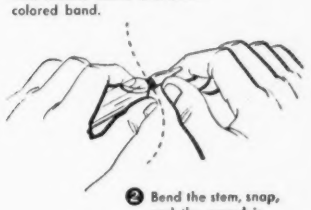

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